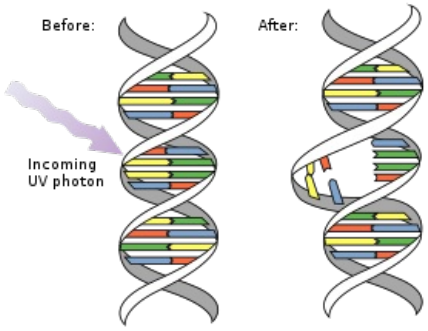
Mutation

A **Mutation** is a **change in genetic information**. It is caused by various influences - the most common mutagens are:

- **physical factors** (UV and ionizing radiation);
- **chemical factors'** (e.g. planar aromatic compounds, strong oxidant, radical initiators);
- **biological factors** (viral infections etc.).

This is a random process, but at the same time it has been proven that in some areas of the genome, mutations occur more often and are referred to as '*hot-spots*.

The mutation, if manifested (see below), can cause serious disease, either various birth defects or neoplasia. However, it is also considered one of the mechanisms of evolution.



Damage of the molecule DNA by UV radiation

Mutations are prevented by DNA repair processes, or so-called ``back mutations*. The increased incidence of mutations occurs with a defect in the genes encoding repair enzymes (mutator genes), which is the basis of various diseases (e.g. Fanconi pancytopenia, xeroderma pigmentosum, Cockayne syndrome).*

Distribution of mutations

According to the cell line affected by the mutation:

- **somatic mutations'** — mutations that are not inherited from parents and cannot be passed on to offspring (they do not affect sex cells);

  > *Mutation in the p53 gene in an intestinal adenoma cell, causing its transition to colorectal cancer.*

- **germ cell mutations** (germline mutations) — mutations that can be inherited from parents and can be passed on to offspring (affect germ cells)

  > *Mutations in the germ cell APC gene causing familial adenomatous polyposis.*

By genome region and expression:

- **coding regions** — mostly cause pathology, depending on what change has occurred (see below);
- **non-coding regions** — usually they do not show up and these are so-called *silent* mutations, if the change did not occur in the following non-coding regions:
  - promoters, enhancers and silencers — affect gene expression; incorrect expression of proto-oncogenes and onco-suppressor genes is then the cause of tumor growth;
  - introns — so-called exonization of an intron can occur and then these are '*splicing* mutations; they stand out in particular.
- **Cryptic** mutations — in regions very similar to splice sites.

According to the change of genetic information:

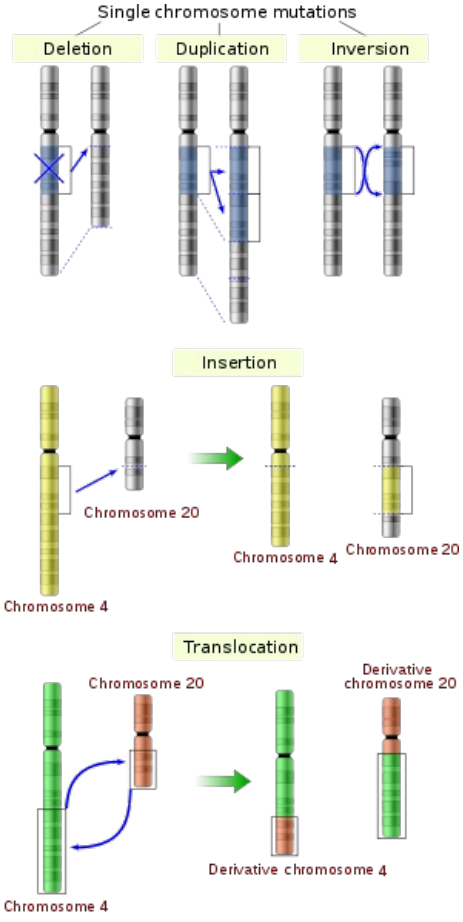
- **point mutations'** — a change in one nucleotide: it can be:
  - *deletions* (analogous to mutations of larger areas),
  - "advertising" (also),
  - *substitution*:
    1. **transition** — change of purine to purine or pyrimidineu to pyrimidine (C → T, T → C, A → G, G → A);
    2. **transversion** — change of purine to pyrimidine or vice versa (A → T, T → A, C → A, A → C, G → T, T → G, G → C, C → G) .

    - manifestations depend on whether the codon with the swapped base codes for the amino acid the same, a different one, or none:

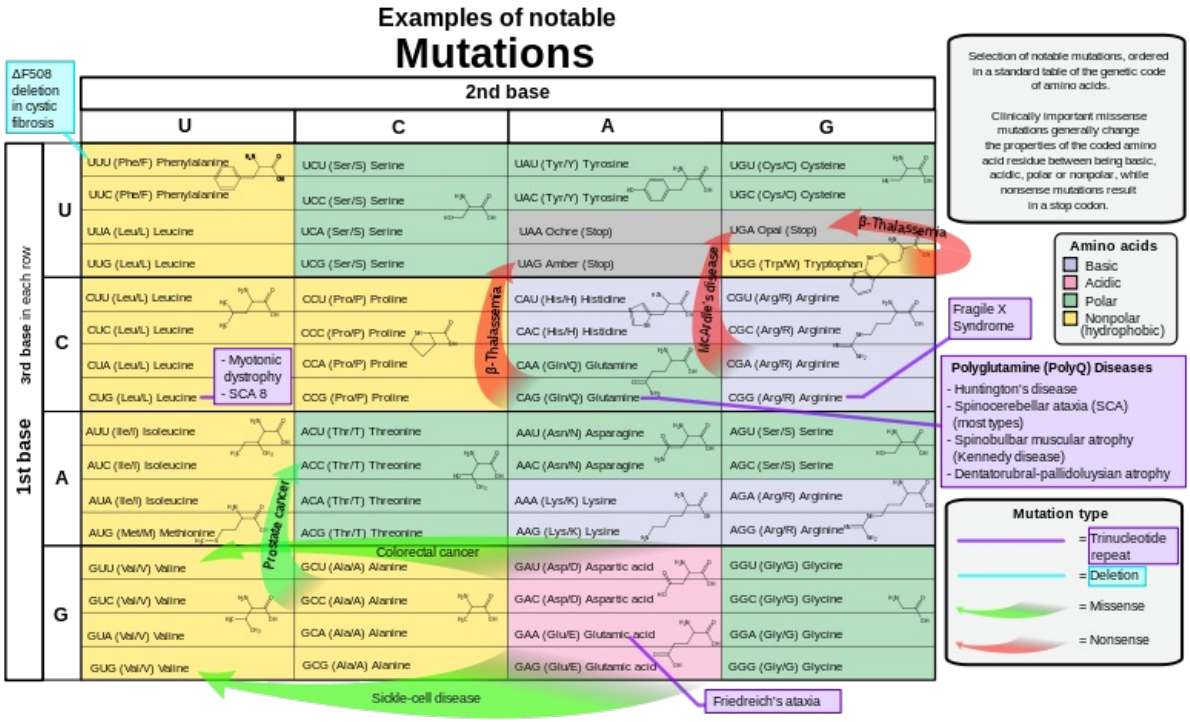
      1. **samesense (silent)** — this is a so-called silent mutation (the same amino acid is included);
      2. **missense** — another amino acid is inserted and the function of the gene product can be changed or even disabled;
      3. **nonsense** — the substitution will cause a new stop codon and thus a shorter gene product, which will probably be non-functional.

Cytosine is the most susceptible to point mutations, which is particularly easily subjected to spontaneous deamination to uracil. Polymerases then misread it as a T, so a transition of a C·G pair to a T·A pair occurs, and the involvement of repair mechanisms can lead to other types of changes. The half-life of cytosine can be around 19 days under certain conditions. Other bases are much more stable, their half-life is around one year.[1]

- mutation of larger areas:
  - **deletion** — causes there to be fewer amino acids in the resulting protein. At the same time, if the number of deleted nucleotides is ``not a multiple of three*, a ``frameshift* occurs - there is a high probability that a newly created stop codon will appear in the vicinity and the protein will be most likely broken;
  - **insertion** — more amino acids are inserted into the resulting protein, similar to deletion, a **frameshift** can occur;
  - **other** structural chromosomal aberrations.



Types of chromosome mutations.



Links

- ws:Mutace

Related Articles

- Tumors
- Apoptosis
- Dynamic mutations
- Evolution
- Birth defects
- (Proto)oncogenes
- Onco suppressor genes
- Mutator genes
- Fanconi pancytopenia
- Xeroderma pigmentosum
- Chromosomal Abnormalities
- Genetic Code

Sources

- SOUKUPOVÁ, Milena – SUM, Francis. *Chapters from medical biology and genetics II.* 1. edition. Prague : Karolinum, 1997. 86 pp. pp. 63 – 66. ISBN 80-7184-581-7.

References

1. – KOMOR, Alexis C. – REES, Holly A.. Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage. *Nature.* 2017, vol. 551, p. 464-471, ISSN 0028-0836. DOI: 10.1038/nature24644 (http://dx.doi.org/10.1038%2Fnature24644).