DNA Repair

DNA repair mechanisms has a very important role in ensuring the stability of genome. They are able to correct about 99% of transcription errors. The frequency of mismatches (incorrect pairing of bases) is about $1:10^7$ nucleotides.

During the day thousands and thousands of changes are occurring. For their reparation, at least one of the DNA chains has to be **intact**. The damaged part can then be resynthesized.

When the mismatch has appeared, it is necessary to cut out the affected region of DNA and to synthesize the new one. If DNA repair mechanisms does not do this, the mutation is transmitted *to the next generation*.

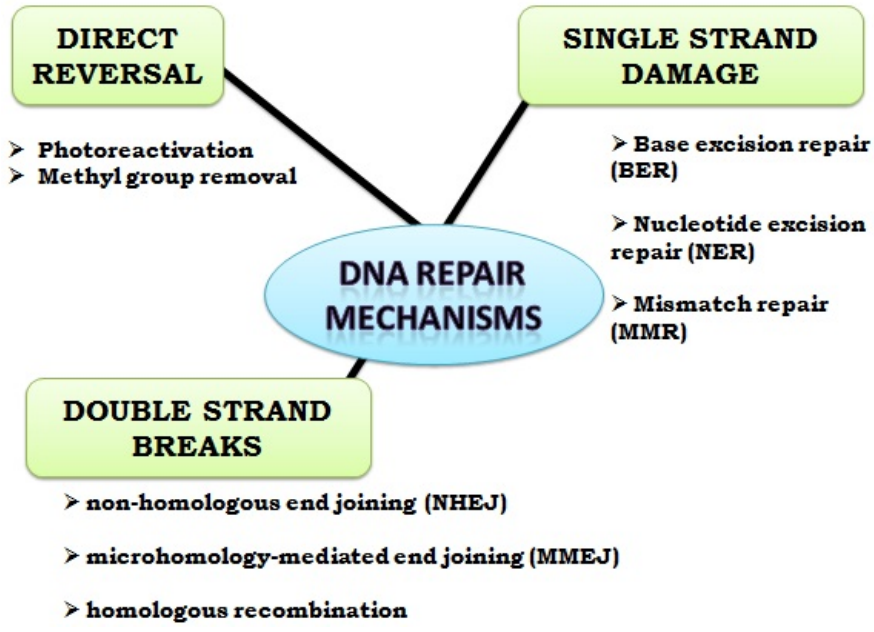
Types of DNA Damage

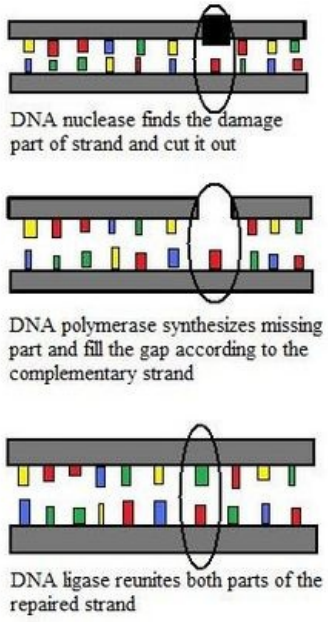
1. **Modification of bases** (loss of amino group)
2. **Mismatches** of the normal bases (failure of DNA replication)
3. **Breaks** of backbone of DNA (the most common cause is radiation)
4. **Cross-links** (linkage between bases)

DNA damage can be caused by:

- *chemical changes* of DNA structure (nitrogen);
- *physical damages* (UV light, radiation);
- *viral damages*.

DNA Repair





DNA repair by enzymes

- DNA damage is recognized by specific enzymes - *nucleases*. The covalent bond is interrupted and the gap occurs.
- *DNA-polymerase* binds to the 3´end of DNA and fills the gap according to the complementary strand.
- *DNA-ligase* reunites the repaired part to the original strand.

Direct Reversal

For this repair mechanism it is *not necessary to break the DNA backbone*. The most common mistakes are caused by **methyl group** ($-CH_3$). It changes C (cytosin) to T (thymin). This problem is solved by enzymes - **glycosylases** - which are able to restore it.

Excision Repair

DNA strand has to be discontinued in order to be repaired.

- **Base Excision Repair** (BER)

- **Nucleotide Excision Repair** (NER)
- **Mismatch Repair** (MMR)

Diseases with Defects in DNA Repair

In past it was discovered that there is a connection between DNA repair defects and developing of **cancer** (especially intestinal cancer). The heredity of repair genes is **recessive**. That means that each person has two different copies of the gene (one from each parent) and it is necessary to damage both of them in order for the disease to occur.

Hereditary Nonpolyposis Cancer Syndome (HNCS)

Disease which is connected with defect of DNA mismatch repair. Normally the incorrect pairing is repaired. But in this case the errors are accumulated in the cells. Tumor suppressive and Protooncogenes are affected too. This leads to *increased risks of developing cancer*. Patients with defect of mismatch repair have typically microsatellite instability.

Xeroderma Pigmentosum (XP)

Patients with XP have an *increased risks of skin cancer*. The reason is inability to repair the cross-linking of pyrimidine pairs, which arise from UV-light influence.

Fanconi anemia, Bloom Syndrome, Ataxia-Teleangiectasia

Autosomal recessive diseases which are connected with *damage of recombination repair genes*. DNA is more sensitive to external agents.

Links

Related articles

- Xeroderma Pigmentosum
- Hereditary Nonpolyposis Cancer Syndrome
- Base

Sources

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