

DNA Repair

DNA damage can result from both endogenous and exogenous causes.

Most DNA damage is repaired before DNA is replicated.

Mutagenic agents (ones that induce mutations) are most effective in causing their damage during S phase of the cell cycle when the new DNA is being synthesized.

The rate of mutations occurring from endogenous (intracellular) causes is termed the basal mutation rate. This is the mutation rate observed in the absence of environmental mutagens and is caused by errors during DNA replication.

Spontaneous tautomeric shifts (changes from one natural structural form to another) in the bases contribute to these errors.

Fortunately, these bases spend very little time in their less stable forms, so mutations caused by tautomeric shift are rare

Mistakes made by DNA polymerase during replication can also cause this type of mutation

Exogenous agents

For example, ionizing radiation, including X-rays and radioactive radiation, is rich with energy and can react with DNA. Ionizing radiation penetrates the whole body and can cause both somatic (cellular) and germ line (oocyte or sperm) mutations.

Some chemicals in the environment, including hydrocarbons, are known to induce mutations.

Hydrocarbons found in cigarette smoke are well-known mutagens.

Oxidative free radicals, produced from internal or external sources, can also induce DNA damage.

Chemicals used in chemotherapy, especially for the treatment of cancer, can also induce mutations.

DNA repair is necessary not only because cells are continuously exposed to environmental mutagens but also because thousands of mutations would occur spontaneously in every cell each day during DNA replication.

A variety of strategies exist for repairing damage to DNA. In most of these cases, the cells use the undamaged strand of DNA as a template to correct the mistakes in DNA.

When both strands are damaged, the cell uses the sister chromatid (the second copy of DNA present in diploid cells) or to an error-prone recovery mechanism.

All types of repair mechanisms are made up of enzymes that follow a general scheme of recognition, removal, repair, and religation.

Depending on the type of damage, different enzymes are employed