

# DNA Repair Mechanisms

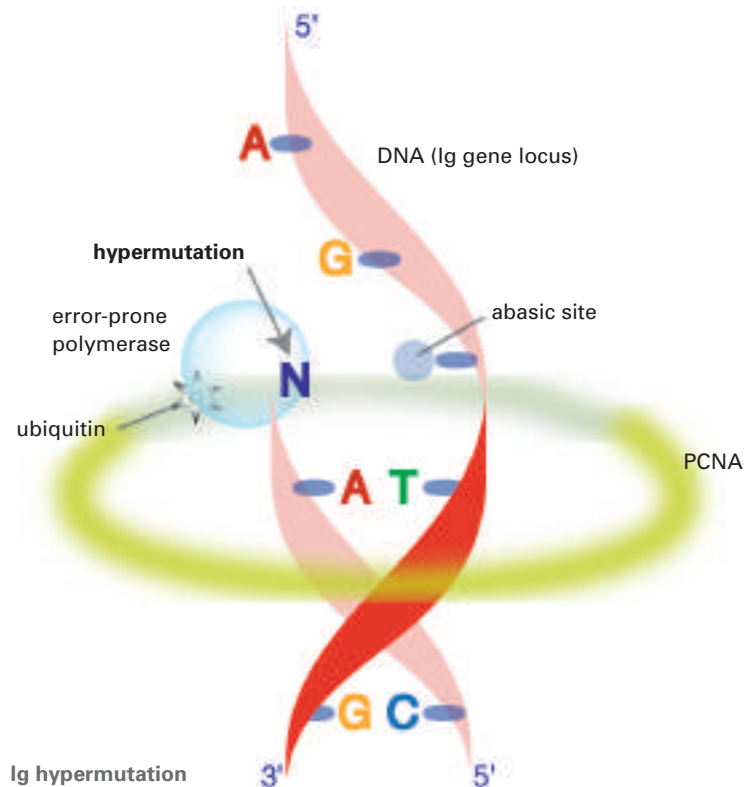
## Optimise One Path in Immune Defence

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Our immune system has to fight off many pathogens everyday. To do this, the B-cells in the immune system produce specific antibodies that are exactly designed for a particular pathogen. Scientists from the GSF-Institute of Molecular Radiobiology have shown for the first time that a molecular mechanism which usually serves the repair of damaged DNA enables cells of the immune system to produce a great variety of antibodies.

Hypermutation, a millionfold increased natural mutation rate – is elicited by a B-cell specific enzyme, AID. This enzyme causes a particular DNA component (a base) to be transformed into a different one. This ‚false‘ base is cut out of the DNA, which leads to a gap. The scientists were able to show that the subsequent steps in hypermutation use a mechanism that is also responsible for the repair of damaged DNA. If the B-cell DNA has gaps, a protein called PCNA is linked with another protein called ubiquitin. This process activates particular emergency repair enzymes which fill the gap. In B-cells this leads to an increased mutation rate because the activated emergency enzymes are likely to build in a different base, out of the four possible, from the original one – leading to a point mutation. Some point mutations result in an increase in the affinity of the resultant antibodies against the pathogen so that they can fight it off more strongly.

The results show that in the B-cells of the immune system, the pathway of the PCNA-ubiquitinisi-



on is so altered that increased mutation rates occur in specific parts of the antibody gene. This is positive on the one hand because it leads to an efficient increase in the antibody variety. On the other hand, there is the risk that in some cases uncontrolled mutations on the ‚wrong‘ genes can contribute to the development of cancer in B-cells.

### Literature:

- Arakawa H. et al.: PLoS Biology 4, 1947-1956 (2006)



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