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Structure and function evolution in DNA repair

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Motivation and Aim: To perform its function as the genetic material, DNA is subject to constant surveillance and repair by many proteins that fix omnipresent DNA lesions, which otherwise could induce mutations or stall replication. Cellular life evolved several distinct enzymatic mechanisms to repair DNA, including direct damage reversal (DR), base excision repair (BER), nucleotide excision repair (NER), mismatch repair (MMR), recombination repair, and non-homologous end joining, assisted by damage prevention and tolerance pathways such as nucleotide pool sanitization and translesion DNA synthesis. DNA repair enzymes employ many structural folds to recognize DNA damage and catalyze the necessary enzymatic reactions. These folds are often closely related to those present in other proteins that are not involved in DNA repair. The evolution of the repair systems in their present forms apparently occurred very early in the history of life, and very little is known about it.
Methods and Algorithms: We have traced the evolutionary relationship of all protein folds in the proteins involved in DR, BER, NER, and MMR, as well as their appearance in the major lineages of life. This allowed as to infer the principal events of appearance and disappearance of certain repair pathways and subpathways in evolution. We have also compared the likely timing of these events with the known chronology of the Earth's chemosphere.
Results: BER likely have evolved from an ancient pathway predating the Bacteria/Archaea split that employed endonucleases universally recognizing non-canonical DNA elements, and diversified involving a variety of DNA glycosylases with the increasing complexity of the Earth's chemosphere, with a major impact from the Great Oxidation Event ~2.4–2.0 Ga. NER had likely independently evolved in Bacteria and Eukaryota, with no traces of this pathway in Archaea. MMR as a complete repair pathway also probably evolved twice but was based on an early system of DNA quality control, possibly related to today's bacterial conjugative DNA transport system. DR, although today represented by several structurally unrelated systems (photolyases, suicidal methyltransferases and oxidative demethylases), can be traced to a very ancient group of radical SAM proteins.
Conclusion: DNA repair systems likely appeared at almost the same time as DNA replication when the main genotoxic factors were replication errors, UV light and ionizing radiation that produced a limited amount of lesions in oxygen-free aqueous solutions. DNA repair greatly diversified with the expansion of the DNA damage repertoire, including metabolic byproducts and reactive oxygen species.
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