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Editorial

Role of DNA damage response in the progression of Disease

The main goal for every organism is simply to reproduce that specific hereditary information as it was and pass it on to the new generation. This must be achieved even as endogenous and environment agents continuously attack the DNA. In response to this threat, several systems of life exist that can find DNA damage, report it and facilitate its repair. Such responses, which affect virtually all cellular processes, are biologically informative because they protect various human diseases. Better knowledge of the mechanisms by which cells respond to DNA damage is helping us to develop new approaches to treatment.

Every cell in the human body experiences tens of thousands of DNA lesions per day. These lesions can inhibit the replication and transcription of the genome and when they are not repaired, or when the repair is faulty, they cause mutations or large-scale genome damage that can compromise cell or organism survival. There are two physiological DNA point mutations where DNA mismatches that are introduced as part of the DNA replication process and DNA strand breaks resulting from abortive topoisomerase I and II activity. Furthermore, about 2000 DNA base lesions per cell per day are produced by hydrolysis and non-enzyme methylation.

These are reactive oxygen species generated as metabolites from oxidative respiration, or emitted in redox-cycling activations of environmental toxicants with Fenton reactions involving transition metals. Reactive oxygen and nitrogen compounds are also generated from macrophages as well as neutrophils at inflammation as well as infected areas. This can encompass chemicals that can form adducts that disrupt base-pairing and/or hinder DNA replication and transcription, lose bases, or create DNA-SSBs. Moreover, when two SSBs occur nearby, or when the DNA-replication machinery encounters a SSB or some other damages, double strand breaks (DSBs) are generated. The enumeration of the above lesions does not include DSBs, which are less common than the other types, are virtually irreparable, and are the most toxic lesions. These all-suggestive mechanisms of DNA damage initiates various infectious diseases and cancers.

Prof. Dr. Ibrahim Hakki Cigerci
Afyonkocatepe University
Afyonkarahisar
Turkey
Email: cigerci@aku.edu.tr