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DISSERTATION SUMMARIES

DNA Replication across the protein-DNA adduct

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In cells, DNA is tightly associated with a variety of proteins that serve both to maintain the structural organization of the genetic material and to coordinate cellular processes including replication, repair, recombination, and transcription. Many endogenous compounds (e.g., metabolites of lipid peroxidation) as well as environmental agents are reactive with both DNA and proteins and thus can produce covalent linkage between these two types of macromolecules.

DNA-protein cross links (DPCs) arise in biological systems as a result of exposure to a variety of chemical and physical agents, many of which are known or suspected carcinogens. These DPCs formed within the cells are usually removed/ cleaved by different cellular mechanisms. The unresolved DPCs can hinder normal functioning of a cell by blocking regular cellular mechanism like DNA replication, transcription and others.

Despite the recognition of the biological significance of DPCs, there are very limited data concerning the repair of these lesions. One possible hypothesis is that the covalent or irreversible bondage of a protein to DNA somehow modifies the whole structure of DNA double helix and hence allowing cell to recognize these DPCs as unnatural nucleotide base pair. . The mechanism how a cell recognizes these DPCs and how these unnatural structures are resolved still remain to be unclear.

Analyses of data generated in prokaryotes revealed the existence of mechanisms of active DPC removal and suggested that more than one repair pathway can be involved in the repair of these lesions. There are couple of possible hypotheses , one being the protein part of the DPCs is to be degraded/ cleaved specifically by a protease, and other Nucleotide excision repair (NER), the repair mechanism in which a damaged base is cleaved and replaces by a regular nucleotide bases. However all the hypotheses lack a proper experimental system. It has been previously reported that DNA replication machinery fails to replicate the DNA in the presence of DPCs revealing the fact of stalling the DNA replication fork at the Site of DPCs. However the exact mechanisms how an ongoing replication fork can bypass these DPCs is largely unknown due to lack of a proper in-vivo or in-vitro experimental system.

In the present study we are developing an in-vitro system to monitor stalling or bypass of DNA replication machinery at the site of DPCs. To accomplish the above task a suicidal DNA substrate is designed to trap a protein irreversibly. DNA binding or DNA modifying proteins can be used to crosslink to the DNA of known sequence. This cross-linked DNA-protein substrate is further purified and can be used as a template for the DNA replication. By using different DNA polymerase including some of the specialized TLS (translesion synthesis) polymerase which specifically replicates damaged DNA; it is possible to check bypass of these DPCs. In future these experiments will also reveal whether a specific polymerase is involved to resolve this kind of naturally occurring cross links.

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Data to the analysis of paleopathology of the Medieval Age in the region between the Danube and Tisza rivers (preliminary report)

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Human paleopathology can be defined as the study of diseases in ancient populations by the examination of human remains (dry skeletons and mummies). However, the anthropological study of diseases in antiquity is very complex and challenging. The interplay of many variables – host resistance, pathogen virulence, cultural practices, ecological settings, malnutrition, crowding – needs to be considered.

The aim is of the investigation is to perform a complete comparative analysis of populations dated to the 11th-17th centuries in the region between the Danube and Tisza rivers based on the presentation and evaluation of the paleopathological alterations.

The following series were included in this study: Nyárlőrinc-Hangár utca, Kalocsa-Szentháromság tér, Kalocsa-Belvárosi Iskola,