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## RESEARCH AREA

Duplication of the genetic material is essential for every living organism. In our laboratory, located at the Institute of Genetics in the Biological Research Centre, we examine the replication of eukaryotic cells. The replicative protein complex works with high speed and high fidelity, but several circumstances can interfere with this process. These could be different damage or structural barriers formed on the template DNA strand. The focus of our research interest is the replication of stable secondary structures, which formation is induced by the endogenous nucleotide sequence of the DNA. There are several types of the stable secondary structures, but our laboratory examines the replication of G-quadruplex (G4) structures. Computational analysis identified that there are more than 700,000 G4 motifs in our genome. Thus, the replication of the G4 in cells is challenging. G4 is a tetramer structure formed by stacking of guanine quartets on single-stranded nucleic acid (DNA or RNA) via Hoogsteen's base pairing. The most well examined form of G4 structures are the telomeres, which ensure the stability of the chromosome ends. Our work focuses on the replication of intrachromosomal G4 structures. Since G4 structures are very stable in physiological conditions, they can block the movement of the replicative machinery, which could lead to genome instability. On this basis, it is expected that the amount of G4-forming sequences is reduced during evolution, but the opposite is true. In E. coli and C. elegans the amount of G4-forming sequences in the genome is 0.42% and 0.89%, respectively, but in human cells 4.17% of the genome can form G4 structures that highlights the important function of G4s in the nuclear processes. Recently it has been described, that G4 structures can regulate the gene expression, the initiation of replication, the recombination and the epigenetic code. Therefore, fast end precise replication of G4 structures is essential, otherwise important nuclear functions might be damaged. For the efficient replication special DNA helicases and regulatory proteins are needed, which can synchronize the action of G4 unwinding DNA helicases and the replication apparat. In our laboratory we examine the function of these regulatory proteins.

## TECHNIQUES AVAILABLE IN THE LAB

Yeast and Caenorhabditis elegans genetic methods Construction of deletion and overexpression mutants, killing curve, genome stability assay), recombinant DNA techniques (DNA isolation and RNA isolation, PCR, cloning, Southern blot), protein purification, characterization of purified proteins, enzyme reactions, characterization of the functional domains of the proteins, Western blot, techniques used for human cell cultures and microscopy.

## SELECTED PUBLICATIONS

Zacheja T., Toth A., Harami G.M., Yang Q, Schwindt E., Kovács M., Paeschke K., **Burkovics, P.** (2020) Mgs1 protein supports genome stability via recognition of G-quadruplex DNA structures. **FASEB J 34:** 12646-12662.

Paeschke, K., **Burkovics, P.** (2020) Mgs1 function at G-quadruplex structures during DNA replication. **Curr Genet 67:** 225-230.

Toth, A., Hegedus, L., Juhasz, S., Haracska, L., **Burkovics, P.** (2017) The DNA-binding box of human SPARTAN contributes to the targeting of Polη to DNA damage sites. **DNA Repair (Amst). 49:** 33-42.

**Burkovics, P.**, Dome, L., Juhasz, S., Altmannova, V., Sebesta, M., Pacesa, M., Fugger, K., Sorensen, C.S., Lee, M.Y., Haracska, L., Krejci, L. (2016) The PCNA-associated protein PARI negatively regulates homologous recombination via the inhibition of DNA repair synthesis. **Nucleic Acids Res 44:** 3176-89.

Smith, R., Lebeaupin, T., Juhász, S., Chapuis, C., D'Augustin, O., Dutertre, S., **Burkovics, P.**, Biertümpfel, C., Timinszky, G., Huet, S. (2019) Poly(ADP-ribose)-dependent chromatin unfolding facilitates the association of DNA-binding proteins with DNA at sites of damage **Nucleic Acids Res 47:** 11250-11267.