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RESEARCH AREA

Stalling of the DNA replication machinery, which occurs as a consequence of encountering unrepaired DNA damage, is a challenge for cells. To rescue the stalled replication fork, different DNA damage bypass mechanisms have evolved that promote replication through DNA lesions. In humans, increased error-prone bypass of DNA lesions causes increased mutagenesis and, as a consequence, a rise in the incidence of cancers. Error-free bypass processes, by contrast, keep mutagenesis low and reduce the frequency of cancers. Our research laboratory is interested in the driving forces and molecular mechanisms of mutagenesis and carcinogenesis. In particular, we investigate the following questions: What are the common roots of evolution and carcinogenesis? What are the molecular mechanisms of chromosomal rearrangements and the formation of point mutations? Why do we observe increased genome instability during carcinogenesis? What is the role of the recently described DNA repair genes in cancer suppression? Why do mutations in certain genes predispose to cancer? Which genes are commonly mutated in cancer, and how do these mutations contribute to tumour development and drug resistance? We investigate these challenging problems using human tissue culture-based reporter systems, next-generation DNA sequencing and purified proteins in reconstituted reaction pathways. Our research provides more insight into the molecular events of genome instability, carcinogenesis and has the potential to identify new tumour markers and drug targets as well as to improve personal cancer treatment.

TECHNIQUES AVAILABLE IN THE LAB

Next-generation DNA sequencing, PCR, qPCR, protein microarray, human tissue culture-based reporter assays such as cell survival, mutagenesis, homologous recombination and various tests, confocal microscopy-based techniques such as protein localization, DNA replication and chromosomal rearrangements, protein overexpression and purification, immunological assays, biochemical enzyme assays, and yeast genetic methods.

SELECTED PUBLICATIONS

Mórocz, M., Zsigmond, E., Tóth, R., Enyedi, M.Z., Pintér, L., **Haracska, L.** (2017) DNA-dependent protease activity of human Spartan facilitates replication of DNA-protein crosslink-containing DNA. **Nucleic Acids Res 45:** 3172-3188.

Chen, J., Ai, Y., Wang, J., **Haracska, L.**, Zhuang, Z. (2010) Chemically ubiquitylated PCNA as a probe for eukaryotic translesion DNA synthesis. **Nature Chem Biol 6:** 270-2.

Blastyák, A., Pintér, L., Unk, I., Prakash, L., Prakash, S., **Haracska, L.** (2007). Yeast Rad5 protein required for postreplication repair has a DNA helicase activity specifi c for replication fork regression. **Molecular Cell 28**: 167-75.

Johnson, R.E., Washington, M.T., **Haracska, L.**, Prakash, S., Prakash, L. (2000) Eukaryotic polymerases ι and ζ act sequentially to bypass DNA lesions. **Nature 406:** 1015-1019.

Haracska, L., Yu, S.L., Johnson, R.E., Prakash, L., Prakash, S. (2000) Efficient and accurate replication in the presence of 7,8-dihydro-8-oxoguanine by DNA polymerase η. **Nat Gen 25:** 458-461.