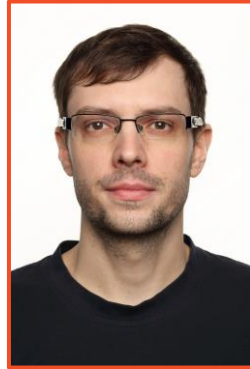


Regular Wednesday IMG seminar



Martin Andrš, Pharm.D., Ph.D.

Laboratory of Cancer Cell Biology

“Reactive oxygen species induce transcription-dependent replication stress in human cells”

Elevated levels of reactive oxygen species (ROS) reduce replication fork velocity by causing dissociation of the TIMELESS-TIPIN complex from the replisome. Here we show that ROS generated by exposure of cells to the ribonucleotide reductase inhibitor hydroxyurea (HU) promote replication fork reversal in a manner dependent on active transcription and formation of co-transcriptional R-loops. The frequency of R-loop-dependent fork stalling also increases after TIMELESS depletion, suggesting that it results due to a global replication slowdown but not ROS per se. In contrast, replication arrest caused by deoxynucleotide depletion does not induce fork reversal but, if allowed to persist, leads to extensive R-loop-independent DNA breakage during S-phase. This work uncovers a link between oxidative stress and transcription-replication interference, which is of crucial importance considering the presence of elevated ROS levels in cancer cells and the fact that transcription-replication conflicts represent a major source of genomic rearrangements found in cancers.

The seminar will be held

on Wednesday 22nd June 2022 at 15:00

in the Milan Hašek Auditorium at IMG

(Institute of Molecular Genetics of the Czech Academy of Sciences, Vídeňská 1083, Prague 4)
