IMG

Institute of Molecular Genetics
of the Czech Academy of Sciences

Regular Wednesday IMG seminar

Anna Huňová Oravetzová

Laboratory of Cancer Cell Biology

"Mechanistic insights into oncogene-induced replication stress"

Active oncogenes promote genomic instability by inducing DNA replication stress, yet the underlying molecular mechanisms remain elusive. We have recently shown that replication fork reversal and chromosome mis-segregation induced by oncogenic RAS (HRASV12) or cyclin E1 overexpression are largely caused by co-transcriptional RNA:DNA hybrids (R-loops) formed during S-phase. Furthermore, we show that replication stress induced by HRASV12, but not cyclin E1, is driven by reactive oxygen species (ROS). This pathway depends on the replisome-associated ROS sensor peroxiredoxin 2 (PRDX2) and triggers the release of the fork acceleration factor TIMELESS from the ongoing replisome. Inhibition of fork reversal in cells overexpressing HRASV12 or cyclin E1 induces unrestrained DNA synthesis mediated by the MUS81 endonuclease, thereby promoting proper chromosome segregation in mitosis. Ultimately, our data indicate that despite playing a protective role during S-phase, persistent reversed forks impair chromosome segregation in mitosis, potentially leading to DNA breaks and chromosomal rearrangements.

The seminar will be held

on Wednesday 10 June 2026 at 15:00

in the Milan Hašek Auditorium at IMG

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