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Vás pozývajú na 133. prednášku v rámci Kuželových seminárov:

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TRANSCRIPTION ON THE EDGE: BALANCING GENE EXPRESSION AND GENOME STABILITY

ktorá sa uskutoční **21. marca 2025** (piatok) o **15:30**
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CV

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Synopsis of the talk

The accurate transmission of genetic information is essential for cellular viability. Since DNA simultaneously serves as a template for replication, recombination, repair, and transcription, conflicts between these processes can arise, potentially leading to genomic instability. A major source of such conflicts is the formation of R-loops – tripartite nucleic acid structures in which nascent RNA hybridises with its complementary DNA strand, leaving the non-template strand unpaired. R-loops can tether RNA polymerases (RNAPs) to chromatin, increasing the risk of collisions with replication and repair machineries. To resolve these conflicts, cells use nucleases and helicases – such as senataxin – to dismantle R-loops and dislodge RNAPs from chromatin.

Recent findings suggest that these pathways are spatially organised into condensates with liquid-like properties. However, how such organisation influences the coordination of transcription with replication, repair, and recombination remains largely unexplored.

In this presentation, I will discuss our contributions to the mechanistic understanding of the crosstalk between transcription and other DNA-centred processes. Special emphasis will be placed on the role of liquid–liquid phase separation in conflict resolution, drawing upon our latest findings, including unpublished work.

Selected publications:

Sebesta, M.[§], Skubnik, K., Morton, W.S., Kravec, M., Linhartova, K., Klapstova, V., Novacek, J., Kubicek, K., Bryja, V., Vacha, R., Stefl, R.[§]. Mechanisms of transcription attenuation and condensation of RNA polymerase II by RECQ5. (*in review*).

Klapstova, V., Sedova, K., Houser, J., **Sebesta, M.** (2025) Distinct Mechanisms of Recognition of Phosphorylated RNAPII C-Terminal Domain by BRCT Repeats of the BRCA1–BARD1 Complex: Insights from Structural and Functional Analyses. *bioRxiv*

Linhartova, K., Falginella, F.L., Matl, M., **Sebesta, M.[§]**, Vacha, R.[§], Stefl, R.[§] (2024) Sequence and Structural Determinants of RNAPII CTD Phase-Separation and Phosphorylation by CDK7. *Nature Communications*, 15, 9163.

Long, Q., Ajit, K., Sedova, K., Haluza, V., Stefl, R., Dokaneheifard, S., Beckedorff, F., Valencia, M.G., **Sebesta, M.**, Shiekhattar, R., Gullerova, M. (2024) Tetrameric INTS6-SOSS1 complex facilitates DNA:RNA hybrid autoregulation at double-strand breaks. *Nucleic Acids Research*, 52, 13036.

Long, Q.*, **Sebesta, M.*[§]**, Sedova, K., Haluza, V., Alagia, A., Liu, Z., Stefl, R., Gullerova, M.[§]. (2023) The phosphorylated trimeric SOSS1 complex and RNA polymerase II trigger liquid-liquid phase separation at double-strand breaks. *Cell Reports*, 42, 113489.

Hasanova, Z., Klapstova, V., Porrua, O.[§], Stefl, R.[§], **Sebesta, M.[§]**. (2023) Human senataxin is a *bona fide* R-loop resolving enzyme and transcription termination factor. *Nucleic Acids Research*, 51, 2818.

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