Katedry genetiky a biochémie PriF UK
a občianske združenie *NATURA*

Vás pozývajú na 109. prednášku v rámci Kuželových seminárov:

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THE DYNAMICS OF NUCLEOPROTEIN FILAMENTS FORMED BY HUMAN RAD51 - DNA RECOMBINASE

ktorá sa uskutoční **24. novembra 2017** (piatok) o **14:00**

v miestnosti CH1-222 Prírodovedeckej fakulty UK

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Lecture annotation:

Cells are under constant genotoxic pressure from both endogenous and exogenous sources. More than tens of thousands of DNA lesions occur in a single human cell every day and they need to be repaired to avoid deleterious mutations, blockage of replication and transcription, and chromosomal breakage. The importance of DNA repair to human health is highlighted by the fact that failure to repair damaged DNA increases the likelihood of developing tumours and other diseases. Homologous recombination (HR) is critical both for repairing DNA lesions in mitosis and for chromosomal pairing and exchange during meiosis. However, some forms of HR can also lead to undesirable DNA rearrangements. Multiple regulatory mechanisms have evolved to ensure that HR takes place at the right time, place and manner. Central to homologous recombination in eukaryotes is the RAD51 recombinase, which forms helical nucleoprotein filaments on single-stranded DNA (ssDNA) and catalyzes strand invasion with homologous duplex DNA. Various regulatory proteins assist this reaction including the RAD51 paralogs, mutations of which predispose to breast and ovarian cancers and Fanconi anemia-like disorders. We recently discovered that a RAD51 paralog complex, functions predominantly downstream of filament assembly by binding and remodelling RAD51-ssDNA filaments to a conformation more proficient for strand exchange. Electron microscopy reconstructions reveal that CX3-induced remodelling alters both RAD51 filament pitch and length to form an open and nuclease-sensitive conformation permissive for strand-exchange.

Selected publications:

Zadorozhny K, Sannino V, Beláň O, Mlčoušková J, **Špírek M**, Costanzo V, Krejčí L (2017). Fanconi-Anemia-Associated Mutations Destabilize RAD51 Filaments and Impair Replication Fork Protection. *Cell Rep* 21(2): 333-340.

Taylor MR*, **Špírek M***, Jian Ma C, Carzaniga R, Takaki T, Collinson LM, Greene EC, Krejci L, Boulton SJ (2016). A Polar and Nucleotide-Dependent Mechanism of Action for RAD51 Paralogs in RAD51 Filament Remodeling. *Mol Cell* 64(5): 926-939. *Co-first author

Taylor MR, **Špírek M**, Chaurasiya KR, Ward JD, Carzaniga R, Yu X, Egelman EH, Collinson LM, Rueda D, Krejčí L, Boulton SJ (2015). Rad51 Paralogs Remodel Pre-synaptic Rad51 Filaments to Stimulate Homologous Recombination. *Cell* 162(2): 271-286.