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Towards a complex view on DNA damage and repair: Epigenetic and spatio-temporal aspects

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Until recently, mainly the genetic and biochemical aspects of processes in the cell nucleus were studied. Nowadays, in the advanced era of 'omics', we have already obtained substantial information on how dozens of proteins interact in the frame of complex cellular signaling pathways and networks. However, additional levels of complexity, like chromatin spatio-temporal organization, have recently emerged as important regulators of fundamental nuclear processes. In this lecture, we will focus on the maintenance of genome integrity, namely the repair of DNA double strand breaks (DSBs). The integrity of the human genome is continuously threatened by intercellular and environmental factors and DSBs represent the most serious DNA lesions; even a single DSB can initiate cell death or cancer when repaired inaccurately. On the other hand, tumor cells are most efficiently killed by DSBs introduced by radiotherapy or chemotherapy. In the last decade, we studied how DSBs, caused by different radiations (high-LET, low-LET) are being induced and repaired. We will discuss the complexity of DSB repair with emphasis on the question of how chromatin structure (nuclear architecture) influences its mechanism and fidelity. Based on the results obtained, we propose a model of the relationship between the higher-order chromatin structure, DSB induction and repair and formation of (carcinogenic) chromosomal translocations.

Biography

Martin Falk has completed his PhD from Masaryk University in Brno, CR. He is the Leader of the Department of Cell Biology and Radiobiology at the Institute of Biophysics of the Czech Academy of Sciences. He has participated in more than 30 papers that concern the role of chromatin structure in regulation of cellular processes. His research interests include DNA damage and repair, carcinogenesis, tumor cells radio-sensitization and radiobiology.

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