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

Vás pozývajú na 101. prednášku v rámci Kuželových seminárov:

Jiří Bártek

Danish Cancer Society Research Center,
Copenhagen, Denmark

GENOME (IN)STABILITY: MECHANISMS AND RELEVANCE FOR CANCER DEVELOPMENT AND TREATMENT

ktorá sa uskutoční **25. marca 2015** (streda) o **15:00**

v prezentačnom centre **AMOS** Prírodovedeckej fakulty UK

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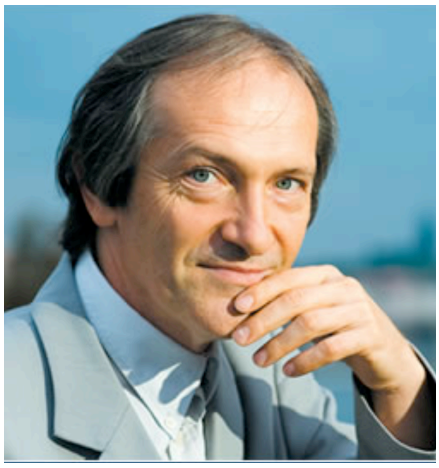

Jiří Bártek is the Head of the Genome Integrity Unit at the Danish Cancer Society Research Center in Copenhagen, Denmark. His work focuses on molecular mechanisms of cell cycle control and genome integrity maintenance, and aberrations of these pathways in human diseases, particularly cancer. He obtained his MD and PhD degrees from Palacky University in Olomouc and Institute of Molecular Genetics of the Czech Academy of Sciences in Prague (both in the Czech Republic), respectively, where he also currently leads Laboratories of Genome Integrity (since 2007). Before moving to his current position in Copenhagen in 1992, he worked as a post-doctoral fellow at the Imperial Cancer Research Fund in London and the German Cancer Research Center in Heidelberg, and as a group leader at the Cancer Research Institute in Brno (until 1990) and Head of Department at the Institute of Hematology in Prague (in 1991-2). Jiří Bártek published over 360 original articles and reviews in the fields of cell and cancer biology, cell cycle regulation and DNA damage response, many of them in top journals such as Nature, Science or Cell. His work is widely cited (~40000 citations; h-Index: 104), and he is the globally most cited Czech researcher, across all disciplines. His discoveries were acknowledged by a number of prestigious awards in Denmark, Czech Republic and elsewhere, he is a member of editorial boards of multiple biomedical journals and a member of EMBO.

Abstract of the lecture:
Biological response to DNA damage is a fundamental biological mechanism ensured through a complex network of DNA damage signaling and effector pathways, the latter including cell-cycle checkpoints, DNA repair and many other aspects of cell physiology. Malfunction of this network predisposes, or contributes to development of life-threatening pathologies including cancer, neurodegeneration, immunodeficiency and premature aging. The lecture will present recent data from our laboratory on both the basic mechanisms of DNA damage response (DDR) and its involvement in cancer pathogenesis and treatments. Highlights from our multiple high-throughput siRNA-based and SILAC-proteomic screens for novel DDR factors, and their functional role in genome maintenance, will also be presented. Furthermore, our recent results on the role of the DDR machinery and its relationship with the ARF-p53 pathways in protection against oncogenes and loss of tumor suppressors, as well as the key role of DNA replication stress in oncogenesis and genetic instability, aneuploidy and hence tumor heterogeneity, will be discussed. In terms of the ARF pathway, our data on a novel function of this important tumor suppressor in regulation of mitochondrial metabolism and the significance of this function to human melanomagenesis, will be presented. Last but not least, exploitation of the DDR defects in human tumors as targets for innovative treatments, and their value as predictive markers to guide individualized cancer therapy, and potential vulnerabilities of cancer stem cells, will be presented. The DDR-targeted therapy will be illustrated by responses of human cancer models to PARP inhibitors and checkpoint kinase inhibitors. These results will be discussed in relation to our most recent discoveries of factors whose loss causes either 'synthetic lethality' (exploited in selective killing of tumor cells) or 'synthetic viability' (enhanced fitness of cancer cells, and hence resistance to treatment), emphasizing the emerging principles of personalized treatment in cancer.

Selected references:
Jackson SP, Bartek J. *Nature*, 461, 1071-8, 2009; Bartkova J et al. *Nature*, 434: 864-70, 2005; Doil C et al. *Cell,* 136, 435-46, 2009; Bartkova J et al. *Nature*, 444: 633-7, 2006; Halazonetis TD, Gorgoulis VG and Bartek, J. *Science,* 319, 1352-5, 2008; Gudjonsson T et al., *Cell* 150: 697-709, 2012; Burrell R et al. *Nature* 494: 492-6, 2013; Watanabe S et al. *Nature Struct Mol Biol* 20:1425-33, 2013; Toledo L et al. *Cell*, 155: 1088-103, 2013; Burrell R et al. *Nature* 501:338-45, 2013; Kumar A et al. *Cell,* 158:633-46, 2014; Xu G et al. *Nature,* in press, 2015.