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

Vás pozývajú na 102. prednášku v rámci Kuželových seminárov:

Prof. Maria Jasin

Memorial Sloan Kettering Cancer Center, New York, USA

PROTECTING THE GENOME BY HOMOLOGOUS RECOMBINATION

ktorá sa uskutoční **27. mája 2015** (streda) o **15:00**

v miestnosti CH1-222 Prírodovedeckej fakulty UK

http://www.naturaoz.org/seminare.html
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Hostiteľ: J. Gregáň, Katedra genetiky

Positions

1978 – 1984 Graduate Student - Paul Schimmel, thesis advisor, Department of Biology, Massachusetts Institute of Technology

1984 – 1985 Post-doctoral Associate - Walter Schaffner, advisor, Institute for Molecular Biology II, University of Zürich

1985 – 1990 Post-doctoral Fellow - Paul Berg, advisor Department of Biochemistry, Stanford University School of Medicine

1990 – present Assistant (1990-1996), Associate (1996-2000), and Full (2000-present) Member, Memorial Sloan-Kettering Cancer Center, Developmental Biology Program (as of 2006); Assistant (1990-1996), Associate (1996-2000), and Full (2000-present) Professor; Weill Graduate School of Medical Sciences, Cornell University

Honors

Massachusetts Institute of Technology: 1978-1979 Phi Kappa Phi Graduate Fellowship; Stanford University**:** 1985-1987 Fellow of the Jane Coffin Childs Memorial Fund;
Memorial Sloan-Kettering Cancer Center: 1990-1993: Frederick R. Adler Chair for Junior Faculty; 1991-1993: Beckman Young Investigator; 1992-1995: Pew Biomedical Scholar; 2000-present: William E. Snee Chair; 2015: Elected to the National Academy of Sciences

Research interests:

Maria Jasin has a longstanding interest in how DNA double-strand breaks (DSBs) are repaired in mammalian cells. To this end, as a beginning investigator, she established approaches to investigate mechanisms of DSB repair in mammalian cells, demonstrating a crucial role for both homologous recombination (HR), also called homology-directed repair, and nonhomologous end-joining (NHEJ). While a role for NHEJ was suspected, a role for HR was completely unexpected; this discovery launched the study of HR as a major area of investigation in mammalian cells. The approaches for these studies involved an endonuclease to generate a DSB in the genome and genetic or molecular assays for DSB repair. She provided plasmids and cell lines to hundreds of labs worldwide to investigate DSB repair pathways and factors; for example, her HR reporter, DR-GFP, has been a standard for HR analysis for ~15 years. A corollary to these discoveries is that an endonuclease-generated DSB is an efficient approach for "gene editing": a DSB repaired by NHEJ will lead to mutagenesis and a DSB repaired by HR will lead to gene targeting. With the approaches established in the lab, she demonstrated that the breast cancer suppressors BRCA1 and BRCA2 are crucial for HR repair, thus implicating HR as a tumor suppression mechanism. These proteins were also found to be essential for the protection of stalled replication forks, a new phenomenon that was uncovered in her studies. She also developed methods to induce de novo oncogenic genomic rearrangements with DSBs, in particular translocations, and determined the contribution of alternative NHEJ and canonical NHEJ to translocation formation in mouse and human cells, respectively.

Maria Jasin's lab has also had a long-stranding interest in germline recombination events and the role of pre-meiotic and meiotic DNA damage in inducing these events. For the last 18 years, Maria Jasin has had a highly productive collaboration with Dr. Scott Keeney on studies of meiotic HR, which is critical for meiotic progression and hence survival of the species. This collaboration led to the discovery of mouse SPO11 which is programmed to introduce numerous DSBs into the genome to induce meiotic recombination. ATM was discovered to regulate DSB numbers and homeostatic control was evident in the conversion of DSBs to meiotic crossovers. These studies determined that HR between the sex chromosomes is differentially controlled. More recently meiotic HR mechanisms were studied using mouse "tetrad" analysis.

The study of both mitotic and meiotic HR is unusual among mammalian researchers and gives a unique perspective on both processes.

Selected references:

Cole F et al., *Nat Genet,* 46:1072-80, 2014; Kass EM et al., Ghezraoui H et al., *Mol Cell,* 55:829-42, 2014; *Proc Natl Acad Sci U S A*, 110:5564-9, 2013; Schlacher K et al., *Cancer Cell*, 22:106-16, 2012; Cole F et al., *Nat Cell Biol*, 14:424-30, 2012.