Katedra aplikovanej informatiky FMFI UK,
Katedry genetiky a biochémie PriF UK
a občianske združenie *NATURA*
v spolupráci so
Slovenskou spoločnosťou pre biochémiu a molekulárnu biológiu

Vás pozývajú na 79. prednášku v rámci Kuželových seminárov:

Leoš Shivaya Valášek
Institute of Microbiology AS CR, Prague

eIF3 rocks: from initiation to termination and back to reinitiation

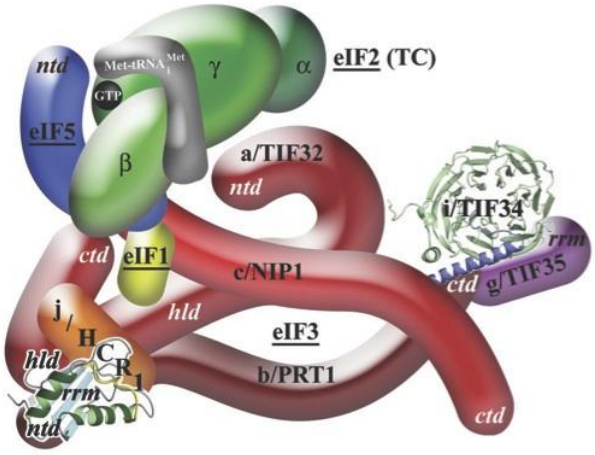
ktorá sa uskutoční **28. apríla 2011** (štvrtok) o **14:00**

v miestnosti **CH1-222** Prírodovedeckej fakulty UK

http://www.naturaoz.org/seminare.html
http://www.naturaoz.org/KuzeloveSeminare.html

Leoš Shivaya Valášek is head of the Laboratory of Regulation of Gene Expression at the Institute of Microbiology AS CR in Prague, where he also serves as the vice chairman of the Executive Board. His laboratory, established in June 2006, investigates a basic concept of translation and various aspects of its control. The studies combine the use of budding yeast *Saccharomyces cerevisiae* and mammalian cells lines, and employ tools of molecular and structural biology, biochemistry and genetics. Dr. Valášek received his M.S. in Genetics and Molecular Biology in 1994 from the Charles University in Prague, and subsequently his Ph.D. in Biochemistry in 1999 from the University of Vienna. He went on to do postdoctoral work in the Laboratory of Gene Regulation and Development, National Institute of Child Health and Human Development, NIH, under supervision of Dr. Alan Hinnebusch. In 2004 he received the ASCR Fellowship of J. E. Purkyne, which is given by the Academy of Sciences of the Czech Republic, and returned back to the Czech Republic to continue with his research on the home ground. In 2005 he was awarded a Wellcome Trust International Senior Research Fellowship, received an NIH FIC Global Health Research Initiative Program Award and became a Howard Hughes Medical Institute International Research Scholar. Dr. Valášek's Wellcome Trust Fellowship was renewed in 2010 and nowadays represents the major funding support of his research. He has published over 30 publications in peer-reviewed journals.

Synopsis of the lecture:



The initiation of translation in eukaryotes requires the coordinated action of at least 12 eukaryotic initiation factors (eIFs). Among them, eIF3 deserves a special attention owing to a broad range of functions that it is believed to promote. Our research aims at addressing molecular details of the key roles that eIF3 performs in close co-operation with other eIFs not only in general translation initiation, but possibly also in termination and recycling, as well as in the gene-specific regulatory mechanism called reinitiation. In the first part of the lecture I will present our most recent data implicating this *bona fide* initiation factor in the regulatory events monitoring the fidelity and timing of termination and ribosomal recycling. Unlike in bacteria, where a specific ribosomal recycling factor exists, this last phase of protein synthesis in eukaryotes has remained a true mystery until a couple years ago, when ABCE1/RLI1 and eIF 1, eIF1A and eIF3 were proposed to drive this process, at least in *in vitro* reconstituted translational systems. Our genetic as well as biochemical data now provide important *in vivo* evidence for the role of eIF3 in termination and suggest a possible mechanism of its involvement. Proper termination followed by incomplete ribosomal recycling, where only the large 60S subunit becomes expelled from the mRNA, represents the critical requirement for one of the most intriguing translational control mechanisms – reinitiation. In the second part of my talk, I will demonstrate the key importance of eIF3 also in this process, which is based on the ability of the post-termination small ribosomal subunit to resume scanning after translating a short upstream open reading frame (uORF) in order to be able to reinitiate at a downstream main ORF. Hence eIF3 forms a molecular bridge across several phases of translation indicating that their mutual "communication" and co-ordination arising from it is a lot broader than initially anticipated.

Recent publications:

- Cuchalová, L., Kouba, T., Herrmannová, A., Danyi, I., Chiu, W.-l., and Valášek, L. 2010. The RNA Recognition Motif of Eukaryotic Translation Initiation Factor 3g (eIF3g) Is Required for Resumption of Scanning of Posttermination Ribosomes for Reinitiation on GCN4 and Together with eIF3i Stimulates Linear Scanning. *Mol Cell Biol* **30**(19): 4671-4686.
- ElAntak, L., Wagner, S., Herrmannová, A., Karásková, M., Rutkai, E., Lukavsky, P.J., and Valášek, L. 2010. The indispensable N-terminal half of eIF3j co-operates with its structurally conserved binding partner eIF3b-RRM and eIF1A in stringent AUG selection. *J Mol Biol* **396**: 1097-1116.
- Chiu, W.-L., Wagner, S., Herrmannova, A., Burela, L., Zhang, F., Saini, A.K., Valasek, L., and Hinnebusch, A.G. 2010. The C-Terminal Region of Eukaryotic Translation Initiation Factor 3a (eIF3a) Promotes mRNA Recruitment, Scanning, and, Together with eIF3j and the eIF3b RNA Recognition Motif, Selection of AUG Start Codons. *Mol Cell Biol* **30**(18): 4415-4434.
- Szamecz, B., Rutkai, E., Cuchalova, L., Munzarova, V., Herrmannova, A., Nielsen, K.H., Burela, L., Hinnebusch, A.G., and Valášek, L. 2008. eIF3a cooperates with sequences 5' of uORF1 to promote resumption of scanning by post-termination ribosomes for reinitiation on GCN4 mRNA. *Genes Dev* **22**(17): 2414-2425.