CeNT CENTRE OF NEW TECHNOLOGIES

UNIVERSITY OF WARSAW

invites to a seminar by

Prof. Robert E. Rhoads

Louisiana State University, USA

Synergistic Application of Organic Chemistry and Biochemistry to Illuminate the Translation and Turnover of Messenger RNA

2nd June 2017 at 12:00 p.m.

Venue: Centre of New Technologies, Banacha 2C,
Lecture Hall 0142 (ground floor)

Host: Prof. Edward Darżynkiewicz

Messenger RNA (mRNA) is central to the transmission of genetic information from DNA to its expression in the form of functional proteins (genotype to phenotype). The presence of a 7-methylguanosine-containing cap structure at the 5'-terminus of mRNA is the chemical signature that distinguishes mRNA from the many other types of RNA in the cell. The cap is involved in virtually all cellular processes in which mRNA participates: synthesis by transcription of DNA, export to the cytosol from the nucleus, intracellular targeting, translation, repression of translation, and degradation. Our laboratory has conducted a long-term collaboration with members of the Institute of Experimental Physics, University of Warsaw, in which we have applied two disciplines, organic chemistry and biochemistry/molecular biology, to advance understanding of how mRNA participates in these cellular processes. This seminar will describe highlights of this collaboration, including: 1) development of methods for measuring binding affinity of cap structures to the translational initiation factor eIF4E; 2) use of cap analogs as inhibitors of protein synthesis and the major decapping enzyme, Dcp2; 3) determining the phosphorylation site of eIF4E and how phosphorylation affects the kinetics of cap binding; 4) discovery and characterization of multiple eIF4E family members in the best characterized animal model organism, *C. elegans;* and 5) developing cap analogs with improved properties with respect to (i) binding affinity for eIF4E, (ii) preventing reverse incorporation during *in vitro* synthesis of mRNA, (iii) translational efficiency *in vitro* and in cultured cells, (iv) intrinsic fluorescence; and (v) resistance to decapping, which is the irreversible step in mRNA degradation, thereby stabilizing mRNA in the cell. We have used cleavage-resistant cap analogs to gain new insight into the pathways by which mRNA is degraded, both for mRNA containing a 3'-terminal poly(A) tract and mRNA containing the 3'-terminal stem-loop characteristic of replicative histones. Finally, mRNAs containing cleavage-resistant caps have been used by others to enhance the priming of naïve T-cells to attack cells expressing cancer antigens, which provides a powerful new approach for cancer immunotherapy.