Katedry genetiky a biochémie PriF UK
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Vás pozývajú na 107. prednášku v rámci Kuželových seminárov:

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TRANSLATIONAL BYPASSING AND OTHER FORMS OF RECODING

ktorá sa uskutoční **6. júna 2017** (utorok) o **11:00**

v miestnosti CH1-222 Prírodovedeckej fakulty UK

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Research:

In decoding the information in some genes to yield their protein products, the standard readout rules are transitorily over-ridden – the phenomenon of recoding. In one type of recoding a proportion of the readout machinery changes reading register resulting in an extra product as well as that derived from standard decoding. Examples include proteins that are essential for HIV and the SARS causing viruses. Another example serves a sensor and effector of regulatory circuit that governs the level of polyamines. In humans, their level is critical for the prevention of certain disease states including cancer and we have been studying analogs with a view to intervention. In yet another case an extensive region of coding sequence is translationally bypassed and its study is providing a novel portal for insights to the functioning of the readout machinery.

A different type of recoding is where the meaning of a coding unit is dynamically changed when it occurs at specific locations. We have found the contextual signals that cause a “stop” in a mammalian virus to instead allow the readout machinery to continue protein synthesis We are actively pursuing the type of “meaning redefinition” utilized by Foot and Mouth disease virus as it appears that its hosts do not use the same mechanism and it could be a target for small molecule intervention.

Though the readout machinery is dependent on proteins for it speed and accuracy, its central functions are mediated by RNA. More broadly, we are alert to the possibility that studies of the readout machinery may provide new clues as to how the process got started in the first place. Not only does RNA play a central role in the readout machinery, it is being found to play unexpectedly diverse roles in the functioning of human and other cells.

Selected recent publications:

1. Atkins JF *et al.* (2017) A [Cu]rious Ribosomal Profiling Pattern Leads to the Discovery of Ribosomal Frameshifting in the Synthesis of a Copper Chaperone. *Mol Cell* 65(2): 203-204.
2. Lobanov AV *et al.* (2017) Position-dependent termination and widespread obligatory frameshifting in Euplotes translation. *Nat Struct Mol Biol* 24(1): 61-68.
3. Atkins JF *et al.* (2016) Ribosomal frameshifting and transcriptional slippage: From genetic steganography and cryptography to adventitious use. *Nucleic Acids Res.* 44(15): 7007-78.
4. Chen J *et al.* (2015) Coupling of mRNA Structure Rearrangement to Ribosome Movement during Bypassing of Non-coding Regions. *Cell* 163(5): 1267-80.
5. Baranov PV *et al.* (2015) Augmented genetic decoding: global, local and temporal alterations of decoding processes and codon meaning. *Nat Rev Genet.* 16(9):517-29.
6. Penno C *et al.* (2015) Productive mRNA stem loop-mediated transcriptional slippage: Crucial features in common with intrinsic terminators. *Proc Natl Acad Sci USA* 112(16): E1984-93.
7. Samatova E *et al.* (2014) High-efficiency translational bypassing of non-coding nucleotides specified by mRNA structure and nascent peptide. *Nat Commun.* 5: 4459.
8. Loughran G *et al.* (2014) Evidence of efficient stop codon readthrough in four mammalian genes. *Nucleic Acids Res.* 42(14): 8928-38.
9. Atkins JF & Baranov PV (2013) Antibiotic re-frames decoding. *Nature* 503(7477): 478-9.
10. Atkins JF, Gesteland GF & Cech TR (eds) (2011) RNA Worlds: From life's origins to diversity in gene regulation. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.