The link between stressed-out mitochondrial ribosomes and cell proliferation

By : Dr. Brendan Battersby

(University of Helsinki, Helsinki, Finland)

Date: 15.10. 2013

Hour: 1:00 p.m.

Room: Institute of Parasitology, Boardroom

Lecture is organised in frame of MODBIOLIN project (FP7, GA 316304).

You're welcome!

Microbes, parasites developing tissues are invaded and eliminated by blood cells, the hemocytes. Assembly of the mitochondrial respiratory chain complexes requires coordinated gene expression and protein synthesis between the nucleo-cytoplasmic compartment and mitochondria. Disruptions in translation elongation can generate organelle and cytoplasmic stresses that can have severe consequences to cellular function independent of the loss of respiratory chain complexes and is a potential compounding factor in the tissue-specificity of mitochondrial diseases. We have recently shown that mitochondrial ribosome stalling can generate a translation stress, which induces a novel mitochondrial ribosome and RNA decay pathway that blocks cell proliferation. Rescue of the stalled mitochondrial ribosomes initiates an acute retrograde signalling response to block cell proliferation and activates a gene expression profile typically associated with an unfolded protein response. Importantly, these events occur prior to any loss of mitochondrial respiratory chain complexes. This mitochondrial ribosome quality control pathway is actively monitored in cells and constitutes an important organelle checkpoint for cell division. Stalling of mitochondrial ribosomes is an underappreciated organelle stress associated with particular classes of pathogenic mtDNA mutations. In cases where tRNA mutations impair aminoacylation, such as the 8344 A>G mutation associated with MERFF, hungry codons will be generated during translation elongation, thus stalling mitochondrial ribosomes. Also, mtDNA deletions will generate abnormal mRNA transcripts with the potential to stall mitochondrial ribosomes and could account for the selective mechanism against mtDNA deletions in proliferating cells. We have identified two genetic factors involved in this ribosome rescue and will present our latest findings elucidating the molecular basis for recognizing and rescuing stalled mitochondrial ribosomes.