Antibiotics a potent translational inhibitors induce the expression of mitochondrial transcripts; an effective mode of treatment for Cancer therapy.

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ABSTRACT:

Mitochondrion is an essential organelle present in virtually all eukaryotic cells. They are vital to the eukaryotic cell as they generate ATP required for cellular processes. Human mitochondria house a circular double-stranded DNA (mtDNA) of ~16,600 base pairs. It encodes 2 rRNAs, 22 tRNAs and 13 protein coding sequences of the ~90 proteins required for the assembly of oxidative phosphorylation (OXPHOS) complexes. Mitochondria are therefore heavily reliant on the nucleus of the cell to provide the remaining proteins required for its function. This mitochondrial translation machinery is of proteobacterial descent, on the basis of bacteria type mito-ribiosome share antibiotic susceptibilities and sequence similarities of ribosomal proteins and RNAs. A number of eukaryotic and prokaryotic translational inhibitors are known that could potentially effect translation of mitochondrial proteins within the mitochondrium. Among these, puromycin is a translational elongation inhibitor that interacts with larger subunit of mammalian mitochondrial ribosome and leads to premature termination of translation. Cycloheximide, eukaryotic translational elongation inhibitor reduces the abundance of cytosolic proteins leading to mitochondrial degeneration by suppression of nuclear encoded mitochondrial targeted proteins. The effect of these translational inhibitors on mitochondrial gene expression is not very well established. Therefore, in this study, we have investigated the effect of translational inhibitors on the expression of human mitochondrial gene expression. We have observed a significant induction in the level of mitochondrial transcripts in response to these antibiotics in both SH-SY5Y (neuroblastoma) and HeLa (cervical) however, the effects on expression of mitochondrial proteins were minimal. This suggests that translational inhibitors might not directly affect the abundance of mitochondrial proteins. Translational inhibitors induce significant effect on mitochondrial gene expression that can be lead to new targeted therapy for treating cancer.

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