The mRNA metabolism pathway regulates mitochondrial homeostasis during ageing in *C. elegans*

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ABSTRACT

Mitochondrial abundance and function are key regulators of lifespan and healthspan in organisms as diverse as the nematode *C. elegans* and humans. Mitochondrial biogenesis and the selective removal of dysfunctional mitochondria via mitophagy are opposing processes that tightly control both the organelle number and homeostasis. Despite the fact that mitophagy has been extensively studied, still little is known about mitochondrial biogenesis. Due to their semi-autonomous nature, mitochondria rely on the expression of both the nuclear and the mitochondrial genome for their biogenesis. The transcription factor SKN-1 and the signaling module AAK-2 are known to promote mitochondrial biogenesis through transcriptional control processes. However, the post-transcriptional mechanisms that regulate nuclear encoded and mitochondrial targeted transcript (NEMTT) expression, required for the organelle biogenesis, remain elusive. To address this issue *in vivo*, we implement a wide range of genetic tools and advanced microscopy techniques. We find that cytoplasmic RNA processing components of the decapping and the CCR-4/NOT complex both physically and functionally associate with mitochondria to regulate the organelle abundance and function. Specifically, we uncover a pivotal role of mRNA metabolism factors in the regulation of local translation of NEMTTs during ageing. Our data underscore the importance of post-transcriptional control of NEMTT expression for lifespan and stress resistance in *C. elegans*. Given the high conservation of the decapping and CCR-4/NOT complex components, this mechanism is probably relevant to pathologies involving mitochondrial abnormalities in humans.