Preferential abundance of MnSOD transcripts during transition from proliferative to quiescent growth state

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Abstract:

The role of the 3'-UTR in regulating mRNA stability and translation has been a subject of increasing interest. Multiple poly-A sites (PAS) on the 3'-UTR results in multiple transcript forms. We hypothesize that there is a preferential abundance of manganese superoxide dismutase (MnSOD) transcripts during transition from the proliferative to quiescent growth state. MnSOD is a nuclear encoded antioxidant enzyme that is located within the mitochondrial matrix. MnSOD plays a vital role in reducing oxidative stress by converting mitochondrial-generated superoxide to hydrogen peroxide. While there are reports of multiple MnSOD mRNAs in different species, only 2 have been reported within humans. The lengths the two mRNA forms are 1.5 and 4.2 kb respectively. These mRNAs have identical coding regions and differ only in the length of the 3'-UTR. Of the multiple forms, the shorter transcript has been shown to correlate with a greater abundance of protein. Our results indicate a higher abundance of the longer transcript during exponential growth, which decreases as the cells reach quiescence. Conversely, the shorter transcript has a lower abundance during exponential growth, which increases during quiescence. The total MnSOD mRNA levels are also lower in exponential cells.This correlates with a two-fold decrease in both MnSOD activity and expression in proliferating cells compared to quiescent cells. These results suggest that lower MnSOD expression in proliferating cells could be due to higher abundance of the unstable MnSOD transcript with the longer 3'UTR. Our results thereby support the hypothesis that preferential abundance of MnSOD transcripts can regulate transition between growth states.