



## **A Cytoplasmic tRNA Synthetase Splice Variant Promotes Mitochondrial Homeostasis**

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The C-Ala splice variant of cytoplasmic (cyt) human (*Hs*) Ala-tRNA synthetase (AlaRS) is encoded by the C-terminus of cytoplasmic AlaRS. Crystal structure analysis of this variant showed it was reshaped to a distinct architecture from that seen in the structure of the C-Ala portion of *A. fulgidis* AlaRS.<sup>1,2</sup> Our further analysis established that, whether ectopically expressed or added exogenously to mammalian cells, *Hs* C-Ala entered the nucleus and mitochondria of mammalian cells. This nuclear and mitochondrial localization correlated strongly with the rescue of stressed mitochondria with defective respiration. Based on additional work, we propose that, at least in part, cyt *Hs* C-Ala has a key role in stabilizing fragile mitochondrial tRNAs and in promoting a transcriptional program that enhances factors needed for mitochondrial homeostasis.