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Titel des Beitrags:
ELAC2 mutations cause a mitochondrial RNA processing defect associated with hypertrophic cardiomyopathy.

Abstract:
The human mitochondrial genome encodes RNA components of its own translational machinery to produce the 13 mitochondrial-encoded subunits of the respiratory chain. Nuclear-encoded gene products are essential for all processes within the organelle, including RNA processing. Transcription of the mitochondrial genome generates large polycistronic transcripts punctuated by the 22 mitochondrial (mt) tRNAs that are conventionally cleaved by the RNase P-complex and the RNase Z activity of ELAC2 at 5’ and 3’ ends, respectively. We report the identification of mutations in ELAC2 in five individuals with infantile hypertrophic cardiomyopathy and complex I deficiency. We observed accumulated mtRNA precursors in affected individuals muscle and fibroblasts. Although mature mt-tRNA, mt-mRNA, and mt-rRNA levels were not decreased in fibroblasts, the processing defect was associated with impaired mitochondrial translation. Complementation experiments in mutant cell lines restored RNA processing and a yeast model provided additional evidence for the
disease-causal role of defective ELAC2, thereby linking mtRNA processing to human disease.