Mol Biol 2018, Volume 7
DOI: 10.4172/2168-9547-C2-006

3rd International Conference on
Molecular Biology & Nucleic Acids
August 27-28, 2018 | Toronto, Canada

Deficient mitochondrial tRNA modifications lead diseases

Min-Xin Guan
Zhejiang University School of Medicine, China

Defects in nucleotide modifications of mitochondrial tRNAs have been associated with several clinical abnormalities including cancer, diabetes, neurological disorders, deafness, and hypertension. To date, 15 types of modifications have been identified in 118 positions in mammalian mitochondrial 22 tRNAs. These nucleotide modifications play a vital role in the structure and function of tRNAs. Core modifications including pseudouridinylation at position 55 at the TΨC loop primary contributed to the structural stability of tRNAs and in some cases, may affect the aminoacylation. These were exemplified by our recent discovery that the loss of pseudouridinylation at position 55 at the TΨC loop of tRNAGlu caused the maternally inherited deafness and diabetes. The modifications at position 37 contributed to the high fidelity of codon recognition and to the structural formation and stabilization of functional tRNAs. Mutations in the nucleotides at position 37 including the tRNAIle 4295A>G, tRNAAsp 7551A>G and tRNAMet 4435A>G mutations were associated with hypertension, diabetes, visual loss, and deafness. These mutations altered their tRNA structures, indicated by an increased melting temperature and electrophoretic mobility of the mutated tRNA compared with the wild-type molecule. These mutations caused significantly decreased efficiency in aminoacylation and steady-state levels of tRNAs. The aberrant tRNA metabolism resulted in the impairment of mitochondrial translation, respiratory deficiency, markedly diminished mitochondrial ATP levels and membrane potential, and increased the production of reactive oxygen species. As a result, the aberrant modification at position 37 of mitochondrial tRNA affected the structure and function of their tRNA and consequently altered mitochondrial function. Our findings provide critical insights into the pathophysiology of maternally inherited disorders, which is manifested by the deficient tRNA nucleotide modification.

gminxin88@zju.edu.cn

Notes: