A novel mitochondrial heteroplasmic C13806A point mutation associated with Iranian Friedreich's Ataxia

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Friedreich's Ataxia (FRDA) is an autosomal recessive neurodegenerative disorder caused by decreased expression of the protein Frataxin. Frataxin deficiency leads to excessive free radical production and dysfunction of chain complexes. Mitochondrial DNA (mtDNA) could be considered a candidate modifier factor for FRDA disease, since mitochondrial oxidative stress is thought to be involved in the pathogenesis of this disease. It prompted us to focus on the mtDNA and monitor the nucleotide changes of the genome which are probably the cause of respiratory chain defects and reduced ATP generation. We searched about 46% of the entire mitochondrial genome by temporal temperature gradient gel electrophoresis (TTGE) and DNA fragments showing abnormal banding patterns were sequenced for the identification of exact mutations. In 18 patients, for the first time, we detected 26 mtDNA mutations of which 5 (19.2%) were novel and 21 (80.8%) were reported in other diseases. Heteroplasmic C13806A polymorphisms were associated with Iranian FRDA patients (55.5%). Our results showed that NADH dehydrogenase (ND) genes mutations in FRDA samples were higher than normal controls (P < 0.001) and we found a statistically significant inverse correlation (r = -0.8) between the number of mutations in ND genes and age of onset in FRDA patients. It is possible that mutations in ND genes could constitute a predisposing factor which affects age of onset and disease progression in combination with environmental risk factors.

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