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Whole-exome sequencing identified compound heterozygous variants in the *TTN* gene causing Salih myopathy with dilated cardiomyopathy in an Iranian family

Mohammad Mahdavi [1], Neda Mohsen-Pour [2], Majid Maleki [1], Mahshid Hesami [3], Niloofar Naderi [1], Golnaz Houshmand [3], Hamid R Rasouli Jazi [4], Hossein Shahzadi [3], Samira Kalayinia [1]

Affiliations

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Abstract

Background: Salih myopathy, characterised by both congenital myopathy and fatal dilated cardiomyopathy, is an inherited muscle disorder that affects skeletal and cardiac muscles. TTN has been identified as the main cause of this myopathy, the enormous size of this gene poses a formidable challenge to molecular genetic diagnostics.

Method: In the present study, whole-exome sequencing, cardiac MRI, and metabolic parameter assessment were performed to investigate the genetic causes of Salih myopathy in a consanguineous Iranian family who presented with titinopathy involving both skeletal and heart muscles in an autosomal recessive inheritance pattern.

Results: Two missense variants of TTN gene (NM_001267550.2), namely c.61280A>C (p. Gln20427Pro) and c.54970G>A (p. Gly18324Ser), were detected and segregations were confirmed by polymerase chain reaction-based Sanger sequencing.

Conclusions: The compound heterozygous variants, c.61280A>C, (p. Gln20427Pro) and c.54970G>A, (p. Gly18324Ser) in the TTN gene appear to be the cause of Salih myopathy and dilated cardiomyopathy in the family presented. Whole-exome sequencing is an effective molecular diagnostic tool to identify the causative genetic variants of large genes such as TTN.

Keywords: Dilated cardiomyopathy; Salih myopathy; TTN; compound heterozygous; titinopathy; whole-exome sequencing.

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