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J Genet Disor Genet Rep 2018, Volume 7
DOI: 10.4172/2327-5790-C1-003

The spectrum of DYSF mutations in Indian dysferlinopathies

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Dysferlin (DYSF) is a 237 kDa transmembrane protein found in sarcolemma, known to facilitate membrane repair in skeletal muscles, muscle differentiation, membrane fusion, etc. The deficiency of DYSF due to mutations is one of the cause for Limb-Girdle Muscular Dystrophy 2B (LGMD2B), Miyoshi Myopathy (MM) and a distal anterior compartment myopathy (DMAT), which are collectively named dysferlinopathy. DYSF gene is located on chromosome 2 (2p13), encompasses 55 coding exons and spans 150 kb of genomic DNA. To evaluate the role of DYSF gene mutation(s) in Indian dysferlinopathies, we have performed both genetic and immunological analyses in 66 clinically defined cases. Western blot analysis of muscle specimens confirmed that all of them had dysferlin deficiency. All the 55 exons of DYSF were sequenced to find mutation(s) that are associated with dysferlinopathies. Sequence analysis of the dysferlin gene in these patients revealed a total of 84 variants. Of these, 51 were novel mutations that include 6 missense mutations, 6 silent mutations, 1 termination mutation, 3 frame-shift mutations, 7 splice site variations and 28 in intronic region and 33 previously reported mutations (5 missense, 7 silent, 1 termination mutation, 5 splice site and 15 intronic region). This is the first extensive study of DYSF mutations in Indian dysferlinopathy samples. We have identified several novel and functionally significant mutation, which can be used as diagnostic markers.

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