Abstract



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# Exome sequencing identifies a novel homozygous variant in NDRG4 in a family with infantile myofibromatosis.

Linhares ND[1], Freire MC[2], Cardenas RG[1], Pena HB[3], Bahia M[4], Pena SD[5].

## Author information

[1]Laboratório de Genômica Clínica, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.
[2]Departamento de Bioquímica e Imunologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.
[3]Laboratório Gene - Núcleo de Genética Médica, Belo Horizonte, Brazil.
[4]Divisão de Gastroenterologia Pediátrica, Hospital das Clínicas da UFMG, Belo Horizonte, Brazil.
[5]Laboratório de Genômica Clínica, Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; Departamento de Bioquímica e Imunologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; Laboratório Gene - Núcleo de Genética Médica, Belo Horizonte, Brazil. Electronic address: spena@dcc.ufmg.br.

## Abstract

Infantile myofibromatosis (IM) is a rare disorder characterized by the development of benign tumors in the skin, muscle, bone, and viscera. The incidence is 1/150,000 live births and the disease is the most common cause of fibrous tumors in infancy. Cases which lack visceral involvement generally have a more benign course, usually with spontaneous regression of the tumors. On the other hand, the prognosis tends to be unfavorable when there is involvement of vital organs, which can lead to significant mortality. The identification of rare variants in genes that may cause IM is the first step towards the possibility of targeted treatments; however, the molecular pathogenesis of IM is poorly understood. In the present study, we report the results of exome sequence analysis of two brothers diagnosed with visceral multicentric infantile myofibromatosis, and their healthy consanguineous parents. In the two brothers we identified novel homozygous variants in NDRG4 gene (N-myc downregulated gene family member 4) and in RLTPR gene (RGD motif, leucine rich repeats, tropomodulin domain and proline-rich containing). The healthy parents were heterozygous for both variants. Consistent with the phenotype of IM, NDRG4 is a tumor-related gene; its expression has been shown to be decreased in numerous tumor types, suggesting that it might be a tumor suppressor gene. Additionally, studies have demonstrated that NDRG4 may have a role in cell survival and tumor invasion. We thus propose that this homozygous variant in NDRG4 may be the causative variant of the autosomal recessive form of IM in the studied family and that it should be investigated in other cases of autosomal recessive infantile myofibromatosis.