Sarcomere Dysfunction in Nemaline Myopathy.

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Abstract

Nemaline myopathy (NM) is among the most common non-dystrophic congenital myopathies (incidence 1:50,000). Hallmark features of NM are skeletal muscle weakness and the presence of nemaline bodies in the muscle fiber. The clinical phenotype of NM patients is quite diverse, ranging from neonatal death to normal lifespan with almost normal motor function. As the respiratory muscles are involved as well, severely affected patients are ventilator-dependent. The mechanisms underlying muscle weakness in NM are currently poorly understood. Therefore, no therapeutic treatment is available yet. Eleven implicated genes have been identified: ten genes encode proteins that are either components of thin filament, or are thought to contribute to stability or turnover of thin filament proteins. The thin filament is a major constituent of the sarcomere, the smallest contractile unit in muscle. It is at this level of contraction - thin-thick filament interaction - where muscle weakness originates in NM patients. This review focuses on how sarcomeric gene mutations directly compromise sarcomere function in NM. Insight into the contribution of sarcomeric dysfunction to muscle weakness in NM, across the genes involved, will direct towards the development of targeted therapeutic strategies.

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