Simposio Internacional: Enfermedades neuromusculares: es el tiempo para el tratamiento
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The system *ubiquitin-proteasoma*

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Laminin α2 chain mutations cause congenital muscular dystrophy with dysmyelination neuropathy (MDC1A). As muscle atrophy is a significant characteristic of MDC1A, we investigated if increased protein degradation is a feature of laminin □2 chain deficient muscles. Indeed, the ubiquitin-proteasome system, which plays a major role in muscle wasting, appeared overactive in MDC1A. Also, the autophagy-lysosome pathway, which is the other major system involved in degradation of proteins and organelles, was dysregulated in MDC1A. Moreover, separate treatments with a proteasome inhibitor (MG-132) and an autophagy inhibitor (3-methyladenine) significantly improved the dystrophic dy^{3K}/dy^{3K} phenotype. These findings indicate that increased activity of the ubiquitin-proteasome system and enhanced autophagic activity are pathogenic in MDC1A and that proteasome and autophagy inhibition, respectively, holds a promising therapeutic potential in the treatment of MDC1A.