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Evidence of mild founder *LMOD3* mutations causing nemaline myopathy 10 in Germany and Austria.

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Abstract

OBJECTIVE: To expand the clinical and genetic spectrum of nemaline myopathy 10 by a series of Austrian and German patients with a milder disease course and missense mutations in *LMOD3*.

METHODS: We characterized the clinical features and the genetic status of 4 unrelated adolescent or adult patients with nemaline myopathy.

RESULTS: The 4 patients showed a relatively mild disease course. They all have survived into adulthood, 3 of 4 have remained ambulatory, and all showed marked facial weakness. Muscle biopsy specimens gave evidence of nemaline bodies. All patients were unrelated but originated from Austria (Tyrol and Upper Austria) and Southern Germany (Bavaria). All patients carried the

missense variant c.1648C>T, p.(Leu550Phe) in the *LMOD3* gene, either on both alleles or *in trans* with another missense variant (c.1004A>G, p.Gln335Arg). Both variants were not reported previously.

CONCLUSIONS: In 2014, a severe form of congenital nemaline myopathy caused by disrupting mutations in *LMOD3* was identified and denoted as NEM10. Unlike the previously reported patients, who had a severe clinical picture with a substantial risk of early death, our patients showed a relatively mild disease course. As the missense variant c.1648C>T is located further downstream compared to all previously published *LMOD3* mutations, it might be associated with higher protein expression compared to the reported loss-of-function mutations. The apparent clusters of 2 mild mutations in Germany and Austria in 4 unrelated families may be explained by a founder effect.

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