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Titel des Beitrags:
A series of West European patients with severe cardiac and skeletal myopathy associated with a de novo R406W mutation in desmin.

Abstract:
Desminopathy is a familial or sporadic cardiac and skeletal muscular dystrophy associated with mutations in desmin. We have previously characterized a de novo desmin R406W mutation in a patient of European origin with early onset muscle weakness in the lower extremities and atrioventricular conduction block requiring a permanent pacemaker. The disease relentlessly progressed resulting in severe incapacity within 5 years after onset. We have now identified three other patients with early onset rapidly progressive cardiac and skeletal myopathy caused by this same desmin R406W mutation. The mutation was present in each studied patient, but not in their parents or other unaffected family members, indicating that the mutation in all four cases was generated de novo. The patients' mutation-carrying chromosomes showed no similarity, suggesting that the R406W mutation has occurred independently. These observations strongly confirm that the de novo R406W desmin mutation is the genetic basis for early-onset cardiac and skeletal myopathy in patients with sporadic disease and indicate that desmin position 406 is a hot spot for spontaneous mutations. The high pathogenic potential of this mutation can be explained by its location in the highly conserved
YRKLLEGEE motif at the C-terminal end of the 2B helix that has a critical role in the process of desmin filament assembly.