

Mutations in *FAM134B*, encoding a novel Golgi protein, cause autosomal recessive severe sensory and autonomic neuropathy

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Sensory and autonomic innervation is important to protect the body from tissue damage. This is highlighted by hereditary sensory and autonomic neuropathy type 2 (HSAN 2B, MIM 613115) characterized by severe mutilations due to impaired nociception and autonomic dysfunction. In a consanguineous family, we mapped the locus of this autosomal recessive condition to chromosome 5p15.1 and subsequently identified homozygous loss of function mutations in *FAM134B*. Analysis of unrelated patients with clinical symptoms compatible with HSAN also revealed homozygous loss-of-function mutations in *FAM134B* in three additional families. In all affected individuals, onset was early with impaired nociception complicated by ulcerations of hands and feet and chronic osteomyelitis leading to progressive acro-osteolysis. *FAM134B* belongs to a family of three uncharacterized genes. We showed that *Fam134b* encodes a cis-Golgi protein of sensory and autonomic ganglia. RNAi mediated knockdown of *Fam134b* by a lentiviral approach resulted in structural alterations of the cis-Golgi compartment and induced apoptosis in a subset of murine primary dorsal root ganglia neurons. The structure of the mammalian Golgi apparatus, composed of numerous membrane stacks, is necessary to maintain its function as the central organelle for modification and distribution of newly synthesized lipids and proteins within the cell. Our findings support a critical role of *FAM134B* in maintaining the elaborate architecture of the organelle and show the significance of the protein in the long-term survival of nociceptive and autonomic ganglia neurons.