Czech family confirms the link between FBLN5 and Charcot-Marie-Tooth type 1 neuropathy.

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Abstract

The article by Auer-Grumbach et al. (2011) reporting that fibulin 5 (FBLN5) mutations are also linked to inherited neuropathies helped us to clarify the cause of autosomal dominant, demyelinating hereditary motor and sensory neuropathy (HMSN I) in our long-time known, but unsolved, Czech family.

Before this study was published, mutations in FBLN5 were associated only with the connective tissue disorder cutis laxa (Loeys et al., 2002; Markova et al., 2003; Lotery et al., 2006; Nascimento et al., 2010) and age-related macular degeneration leading to vision loss in those aged >50 years (Stone et al., 2004; Lotery et al., 2006). Auer-Grumbach et al. (2011) were the first to describe a large family with demyelinating Charcot-Marie-Tooth (CMT1) and linkage with the interval on chromosome 14. Subsequent resequencing of this region revealed only one novel variant c.1117 C > T (p.R373C) segregating with the disease in the family. Additional screening of 112 patients with Charcot-Marie-Tooth disease showed two other sequence variations in two patients with pure motor neuropathy and hyperelastic skin. The linkage with log of odds score >3.31 indicates the FBLN5 mutation as highly probably causal for HMSN I, but no functional study to confirm this was performed, and no other study on FBLN5 mutations in a family with HMSN has been published to date. This Austrian HMSN I family is the only one reported worldwide.

We report a second family with non-syndromic inherited demyelinating motor and
sensory neuropathy (HMSN I) with FBLN5 mutation and confirm FBLN5 mutations as the new cause of HMSN I.