**Abstract**

Distal hereditary motor neuropathy type V (dHMN-V), Charcot Marie Tooth Syndrome type 2D (CMT2D) and Silver Syndrome are phenotypically overlapping diseases which can be caused by mutations in the gene encoding glycyl tRNA synthetase (*GARS*) and in the Berardinelli-Seip Congenital Lipodystrophy 2 gene (*BSCL2)*. To study the frequency and distribution of mutations in the *GARS* and *BSCL2* genes we screened 33 unrelated sporadic and familial patients diagnosed as either dHMN-V, CMT2D or Silver Syndrome. The majority of patients exhibited predominant hand muscle involvement. Several patients additionally presented with spastic paraparesis of the lower limbs. Further, a series of 68 individuals with unclassified dHMN was screened for mutations in exon 3 of the *BSCL2* gene. From the 33 probands 4 patients carried known mutations in exon 3 of the *BSCL2* gene and in one patient we detected a novel mutation in exon 3of the *GARS* gene. In the series of unclassified dHMN cases no mutations were detected.

Our data confirm that most likely only two mutations (N88S, S90L) in exon 3 of *BSCL2* lead to a dHMN-V or Silver Syndrome phenotype whereas *BSCL2* mutations have not yet been identified in CMT2D patients. Mutations in the *GARS* gene are not a common cause of dHMN-V and CMT2D and might not be associated with Silver syndrome. We would therefore suggest that a genetic testing of dHMN-V patients should begin with screening of exon 3 of the *BSCL2* gene. Screening of *GARS* is useful in patients with CMT2D and dHMN-V cases negative for mutations in *BSCL2* whereas it might not be reasonable in Silver syndrome patients.

The diagnostic yield gained in the series of 33 probands was 12.1 % for *BSCL2* mutations and 3.0 % for *GARS* mutations. This rather low frequency of mutations in the *BSCL2* and *GARS* genes in dHMN-V, CMT2D and Silver syndrome patients strongly points to further genetic heterogeneity of these related disorders.