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Mutation spectrum and phenotypes of thirty Portuguese families with autosomal recessive limb-girdle muscular dystrophy
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A group of 65 patients, comprising 59 apparently unrelated families, were screened for mutations in the sarcoglycan (SG) genes, as well as in the CANP3 and DYSF genes. A total of 30 families (36 patients) were characterized at the molecular level and found to fall into the following groups: 4, LGMD2A; 15, LGMDC; 8, LGMD2D; 3, LGMD2E. Four new mutations were identified: two in the α-SG and two in the β-SG genes. Only two mutations, namely Δ521-T and C283Y, accounted for all of the γ-sarcoglycanopathies. The former was found on two genetic backgrounds for the D12S232 marker, even among five unrelated patients from the Island of Madeira. C283Y was found only and in all patients of Gypsy ethnicity, always on the same D13S232 allelic background, supporting the founder hypothesis. The α-SG mutation R77C was also particularly prevalent, accounting for 11 of the 60 mutated chromosomes (18.3%). Marked phenotypic heterogeneity was observed between and within the families presenting this mutation in homozygosity. As a whole, the LGMD2D group presented the widest phenotypic spectrum, while those with β-sarcoglycanopathies, γ-sarcoglycanopathies (with a few striking exceptions) and calpainopathies, were generally more homogeneous.

Keywords: Autosomal recessive muscular dystrophy; New mutations; Phenotypes