**Genetic profile of LAMA2-related muscular dystrophy patients in a large Brazilian cohort**

**Introduction:** LAMA2-related muscular dystrophy (LAMA2-RD) is an autosomal recessive disease caused by mutations in the *LAMA2* gene. It varies in severity, from a severe form of congenital muscular dystrophies (CMD-LAMA2) - in which most patients never achieve walking capacity - to a more rare and less severe form of limb-girdle muscular dystrophy (LGMD-23).
**Objective:** We aimed to describe and establish genotype–phenotype correlations in a large Brazilian cohort.
**Methods:** Clinical and genetic data of LAMA2-RD patients enrolled from four research centers between March 2018 and January 2023 were collected and analyzed.
**Results:** One hundred and five patients were included: 79 (75.2%) patients never achieved walking capacity and 26 (24.8%) patients were able to walk.
84 patients were submitted to brain MRI, and from those 12 patients (14.2%) presented with cortical malformations (polymicrogyria, lissencephaly-pachygyria, and cobblestone),12 patients (14.2%) presented with epilepsy, and 8 (9.5%) had intellectual disability. We found 42 distinct mutations and twenty-two variants were novel (52%). The top three high-frequency disease-causing variants in Brazilian patients were: 1) c.1255del (p.Ile419Leufs*4) in 20 patients; 2) c.2461A>C (Thr821Pro) in 15 patients and 3) c.3976C>T (p.Arg1326*). The frameshift variant c.1255del (p.Ile419Leufs*4) was never published and is probably a founder mutation in Brazil, with all patients unable to walk. All the 15 patients with at least one c.2461A>C (Thr821Pro) mutation were able to walk. Null variants were more frequent in LAMA2-CMD (56.9%) than in LGMDR23 (21.4%), while missense disease-causing variants were more frequent in LGMDR23 than in LAMA2-CMD (*P* = .0072; OR:6.48)
**Conclusions:** This study provides better understanding of genotype–phenotype correlations in LAMA2-related muscular dystrophy and supports therapeutic targets for future research.