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Exploring the FKRP Gene in Calabrian Patients with Duchenne/Becker-like Phenotype

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Background: Pathogenic variants localized in the gene coding for the Fukutin-Related Protein (FKRP) are responsible for Limb-Girdle Muscular Dystrophy type 9 (LGMDR9), Congenital Muscular Dystrophies type 1C (MDC1C), Walker-Warburg Syndrome (WWS) and Muscle-Eye-Brain diseases (MEB). LGMDR9 is the fourth most common hereditary Limb Girdle Muscular Dystrophy in Italy. LGMDR9 patients with severe disease show an overlapping Duchenne/Becker-like phenotype and may have secondary dystrophin reduction on muscle biopsy.
Material and Methods: We conducted a molecular analysis of the FKRP gene by direct sequencing, in 153 Calabrian patients with Duchenne/Becker phenotype without confirmed genetic diagnosis.
Results: Mutational screening of the patients (112 men and 41 women, aged between 5 and 84 years), revealed pathogenic variants in 15 of 153 patients analyzed. The Arg143Ser variant has a slightly higher frequency than the Leu276Ile variant commonly described as the most frequent in the European population.
Conclusion: The results obtained, demonstrate that the Duchenne/Becker-like phenotype is frequently determined by mutations in the FKRP gene in our cohort and highlight the importance of considering LGMDR9 in the differential diagnosis of Duchenne/Becker muscular dystrophy in Calabria. Finally, this study, which to our knowledge, is the first conducted on Calabrian sample will contribute to the rapid identification and management of LGMDR9 patients.