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SHORT REPORT

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De novo variants and recombination at 4q35: Hints for preimplantation genetic testing in facioscapulohumeral muscular dystrophy

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Abstract

Facioscapulohumeral muscular dystrophy (FSHD) has been associated with the deletion of an integral number of 3.3 kb units of the polymorphic D4Z4 repeat array at 4q35. The prenatal identification of this defect can be carried out on chorionic villi or amniocytes, whereas preimplantation genetic testing for monogenic disorders (PGT-M) requires molecular markers linked to the D4Z4 allele of reduced size. In this context the reliability of this association is crucial. To test the informativeness of the nearby polymorphic markers we investigated recombination at 4q35 using the polymorphic markers D4S1523, D4S163 and D4S139 positioned at 0.55, 0.5 and 0.21 Mb proximal to the D4Z4 array respectively. We determined the probability of recombination events to occur in the D4Z4-D4S1523 interval considering 86 subjects belonging to 12 FSHD families and found a recombination frequency of 14% between D4Z4 and D4S1523. Our study also revealed the occurrence of de novo variants and germline mosaicism. These findings highlight the recombinogenic nature