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### FRAGILE-X PORTUGUESE PATIENTS: A COMMON ANCESTOR?

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The Fragile X Syndrome (FXS) is the most common form of mental retardation, caused by an expansion of a highly polymorphic and potentially unstable triplet-repeat (CGG) located in the 5'-untranslated region of *FMR1* gene. The mechanism underlying the expansion remains unknown although its propensity to expand to a pathogenic mutation depends on the repeat length. Four types of *FMR1* alleles have been identified: normal (6-49 CGGs), intermediate/grey-zone (50-58 CGGs), pre-mutation (58-200 CGGs) and full mutation (>200 CGGs) (EMQN guidelines). Evidence for linkage disequilibrium between the Fragile X expansion and haplotypes around *FMR1* locus have been reported in several populations, which is in line with the occurrence of a number of ancestral mutational events. A study concerning normal and Fragile X individuals of Portuguese origin revealed that haplotype distribution was significantly different in both groups, which suggested the existence of specific founder mutations in Portuguese patients. This study was now extended using the polymorphic markers DXS458 and FRAXAC1, in a further 22 unrelated fragile X and 70 control chromosomes. The pattern and heterozygosity observed in the control population was identical to that previously described, with the haplotype C-7 being the most frequent. Additionally, the high frequencies of A-2 and C-5 haplotypes in the Fragile X population were in agreement with previous studies. Interestingly, we have identified a different high-risk haplotype (A-5) that seems unique to the Fragile X Portuguese population. These findings widen the diversity of haplotypes associated with Fragile X, as opposed to control chromosomes. On the one hand, the high frequency of these haplotypes suggests the existence of specific founder mutations in Portuguese patients, but on the other hand its higher heterozygosity does not support the model of a Fragile X founder chromosome. Ongoing work seeks to determine whether these findings reflect the recombination between different haplotypes, the instability in microsatellite loci or the existence of a specific Portuguese common ancestor(s).