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In silico analysis of *FMR 1* gene to identify and prioritize the single nucleotide polymorphismsfor Fragile X syndrome

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Fragile X Syndrome (FXS), the most common form of inherited mental retardation is due to the expansion of CGG repeats present in *FMR 1* gene. In our previous study, 16 (5%) out of 298 children presenting to the specialist mental health clinic at the Lady Ridgeway Hospital with learning difficulties showed FXS like phenotype without repeat expansions. In literature, it is reported that 1% of the individuals with FXS phenotypic features are negative for repeat expansions. Furthermore, 58 known polymorphisms have been identified in *FMR 1* among 963 mentally retarded males without repeat expansions.*FMR I* gene contains a total of 471 Single Nucleotide Polymorphisms (SNPs). However, these SNPs are not prioritised for FXS. The objective of the present study was to prioritize these SNPs in the *FMR 1* gene to identify the most suitable SNP markers for genotyping.

SNP prioritization was carried out utilizing freely downloadable bioinformatics tools. Initially validated SNPs were selected from the SNP data base (dbSNP). Thereafter, SNPs with Minor Allele Frequency (MAF) 5% or >5% were selected among the validated SNPs. Finally, putative functional effects were determined in both coding and non coding SNPs among the selected SNPs. Function Analysis and Selection tool for SNP (FASTSNP) was used as the primary tool to prioritize SNPs according to functional effects and all other software such as PupaSuite 2, MATCH^{TM}, GeneCards V3 and Human Splice Finder (HSF), were used as additional tools to gain a full overview. Among the 471 SNPs, a set of 26 SNPs were selected as the optimum candidates. Among the 26 SNPs, three were presented in the coding region (X147010320, X147011480 and X147030322) that encode a motif of FMRP and regulate splicing. One SNP was in 5' upstream region (X146991532) and acted as a promoter regulatory region. The other SNPs were in intronic regions and acted as intronic enhancers. The SNP priority list constructed for *FMR 1* gene would act as a guideline for future genotyping studies carried out with the *FMR 1* gene to examine the FXS like phenotypes.

Keywords: Fragile X syndrome, SNP, *In silico analysis,* Fragile X like phenotypes, *FMR 1* gene

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