Absence of expression of the FMR-1 gene in fragile X syndrome.

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Abstract

We previously reported the isolation of a gene (FMR-1) expressed in brain at the fragile X locus. One exon of this gene lies within an EcoRI fragment that exhibits length variation in fragile X patients. This exon also contains the CGG repeat within the CpG island hypermethylated in fragile X patients. To study the involvement of the FMR-1 gene in the fragile X syndrome, its expression was studied in lymphoblastoid cell lines and leukocytes derived from patients and normal controls. FMR-1 mRNA was absent in the majority of male fragile X patients, suggesting a close involvement of this gene in development of the syndrome. Normal individuals and carriers all show expression. The methylation status of the BssHII site at the CpG island was also studied by Southern blot analysis of DNA from patients, carriers, and controls. The minority of fragile X affected males that show expression of FMR-1 demonstrated an associated incomplete methylation of the BssHII site.

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