

Physical linkage of the fragile site FRA11B and a Jacobsen syndrome chromosome deletion breakpoint in 11q23.3

Abstract

Autosomal fragile sites, unlike their X-linked counterparts, are not known to be associated with disease. However, one case report has highlighted a possible relationship between the inheritance of a rare folate-sensitive fragile site in band 11q23.3 (FRA11B) and the chromosome 11q23-->qter deletion in Jacobsen (11q-) syndrome. The mother and brother of the reported Jacobsen syndrome child are FRA11B carriers, suggesting that in vivo breakage at the fragile site during early development could have given rise to the chromosome deletion. We have tested this hypothesis by high resolution physical mapping of FRA11B and of the deletion chromosome breakpoint in the Jacobsen syndrome patient. A detailed restriction map of 600 kb of human chromosome band 11q23.3 has been assembled which covers the PBGD, CBL2 and THY1 genes. FISH experiments with YACs and cosmids from this region have localised FRA11B to an interval of approximately 100 kb containing the 5' end of the CBL2 gene, which includes a CCG trinucleotide repeat. This class of repeat is expanded in the four cloned examples of fragile site and therefore the CBL2 repeat is a candidate for the location of FRA11B. Further, it is shown that the chromosomal deletion breakpoint of the Jacobsen syndrome child maps within the same interval as the fragile site. The breakpoint has apparently been repaired and stabilised by the de

novo addition of a telomere. These data are consistent with a role for an inherited fragile site in the aetiology of a chromosome deletion syndrome.

Jones C, Slijepcevic P, Marsh S, Baker E, Langdon WY, Richards RI, Tunnacliffe A. Physical linkage of the fragile site FRA11B and a Jacobsen syndrome chromosome deletion breakpoint in 11q23.3. *Hum Mol Genet.* 1994 Dec;3(12):2123-30. doi: 10.1093/hmg/3.12.2123. PMID: 7881408.