

*Short report*

# DMD carrier detection in a female with mosaic Turner's syndrome

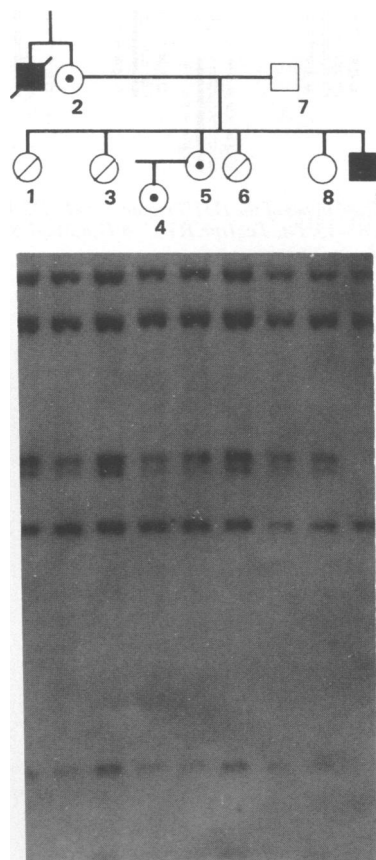
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We are at present trying to identify DMD carriers by gene dosage analyses in those DMD families where the patient exhibits a deletion within one of the DMD cDNA clones.<sup>1</sup> In the study of one such family using probe 8, a deletion of the 1.25, 3.8, 1.6, and 3.7 kb *Hind*III fragments was seen in a boy with DMD. Visual inspection of the intensity of the 3.8 and 3.7 kb bands diagnosed subjects 1, 3, and 6 as non-carrier females and subjects 2, 4, and 5 as DMD carriers (fig 1). However, the pattern in subject 8 was difficult to determine as the bands exhibited an intensity between the normal male and the non-carrier female pattern (fig 1).

In spite of the careful measurements of DNA concentration usually carried out when using cDNAs for DMD carrier detection, we studied this family again and obtained the same results. Having requested additional information from the hospital that sent us the samples, it was reported that subject 8 had had previous cytogenetic study of peripheral blood which showed 80% 45,X, 20% 46,XX (mosaic Turner's syndrome).

Subsequently, we performed complete haplotyping with intra- and extragenic probes in this family (fig 2). In patient 8, alleles of paternal origin show normal intensity, whereas the faint bands visible only with informative markers correspond to the X chromosome of maternal origin.

The results of these studies confirmed the DMD carrier diagnosis done with cDNA probes in subjects 1, 2, 3, 4, 5, and 6. On the autoradiograph obtained after the usual exposure time, the DNA sample



*Figure 1 HindIII fragments detected by cDNA probe 8. Dosage analysis on visual inspection showed reduced intensity of the bands deleted in the male patient and in subjects 2, 4, and 5 and normal band intensity in subjects 1, 3 and 6. Subject 8 shows an intensity of the 3.8 and 3.7 kb bands between normal male and normal female.*

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corresponding to subject 8 appeared to be homozygous for all the polymorphic markers used. However, keeping in mind the existence of the Turner mosaic, we increased the exposure time of the filters to two weeks. Under these conditions, subject 8 showed

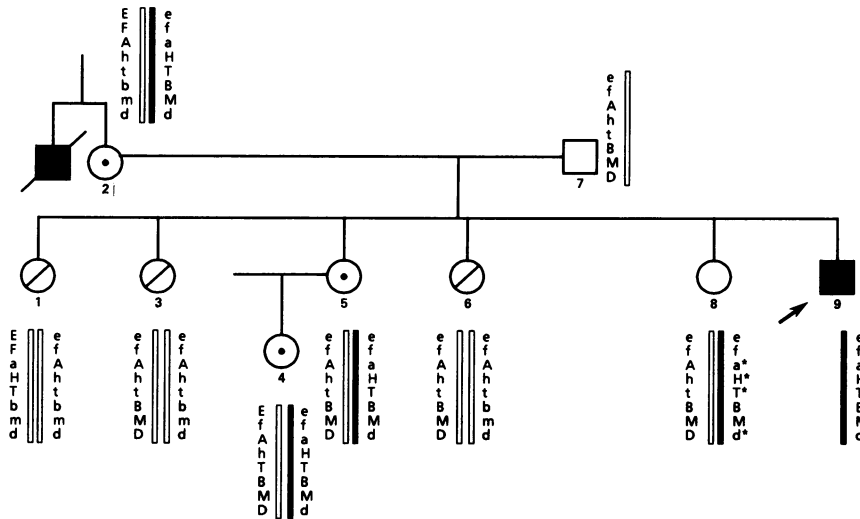


Figure 2 Haplotypes of the DMD region (*PvuII/D2:Ele;PstI/99.6:F,f;EcoRV/p20:A/a;MspI/p20:H/h;TaqI/pERT87-15:T/t;TaqI/pERT87-8:B,b;MspI/87-1:M/m;TaqI/XJ23:D,d*). \*=faint alleles. Subjects numbered as in figure 1.

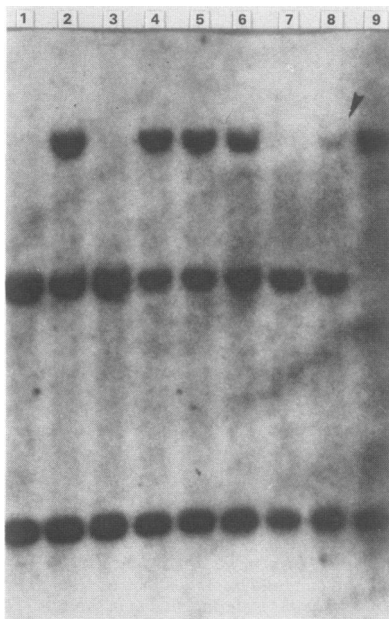


Figure 3 Southern blot analysis of p20 *MspI* RFLP. An arrow marks the low intensity allele corresponding to the X chromosome involved in the Turner mosaic (see text). The track numbers correspond to the numbered subjects in figure 1.

bands of very low intensity with some markers (*MspI/p20*, *TaqI/87.15*, *TaqI/XJ23*) (fig 3), which allowed us to identify the at risk haplotype in this woman. The low intensity of the polymorphic alleles and the intermediate intensity seen with probe 8 can be explained if the X chromosome that carries the DMD deletion is that involved in the Turner mosaicism.

Although the aim of this study was to detect DMD carrier females in this family, the finding reported here prompts us to emphasise two points: as cDNA probes are now often used in a large number of laboratories for DMD carrier detection,<sup>2,3</sup> we suggest that when confronted with unusual band intensities, a karyotypic abnormality should be considered. In addition, laboratories dealing with blood samples alone need as much clinical and cytogenetic data as possible, in order to make a better molecular diagnosis.

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- 2 Darras BT, Koenig M, Kunkel L, Franke U. Direct method for prenatal diagnosis and carrier detection in Duchenne/Becker muscular dystrophy using the entire dystrophin cDNA. *Am J Med Genet* 1988;29:713-26.
- 3 Speer A, Spiegler AWJ, Hanke R, et al. Possibilities and limitation of prenatal diagnosis and carrier determination for Duchenne and Becker muscular dystrophy using cDNA probes. *J Med Genet* 1989;26:1-5.