EXHIBIT 12



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United States Patent [19]

Caskey et al.

[54] DIAGNOSIS OF THE FRAGILE X SYNDROME

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Tex.

[*] Notice: This patent is subject to a terminal dis-

claimer

[21] Appl. No.: 07/705,490

[22] Filed: May 24, 1991

[52] **U.S. Cl.** 435/6; 435/91.2; 536/23.1;

536/24.33; 536/24.1

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using somatic cell hybrids with Fragile X breakpoints for identifying the Fragile X site.

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Vincent, et al., "Abnormal pattern detected in Fragile-X patients by pulsed-field gel electrophoresis" *Nature* 349:624–626 (1991). This paper describes long-range restriction mapping experiments that determined Fragile X specific hypermethylation of a CpG island in numerous patients.

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[57] ABSTRACT

A sequence of the FMR-1 gene is disclosed. This sequence and related probes, cosmids and unique repeats are used to detect X-linked diseases and especially the fragile X syndrome.

4 Claims, 10 Drawing Sheets

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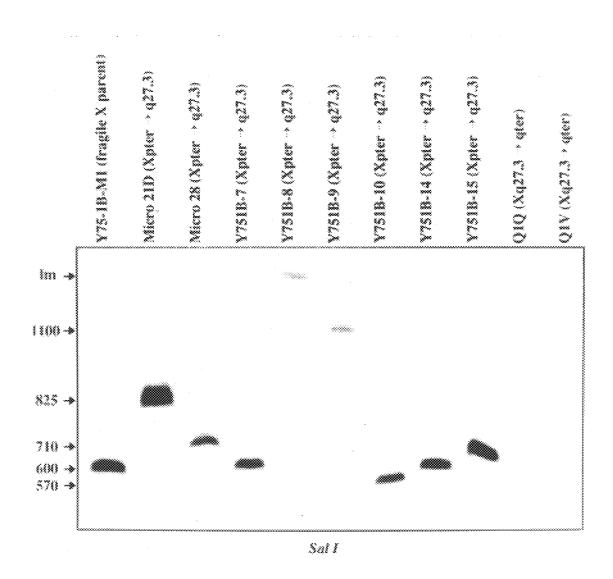


Figure 1

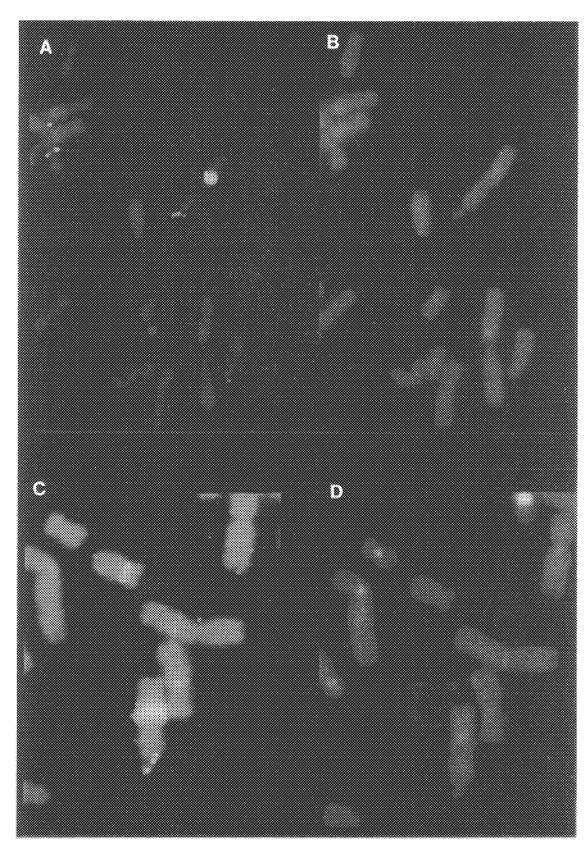


Figure 2

U.S. Patent

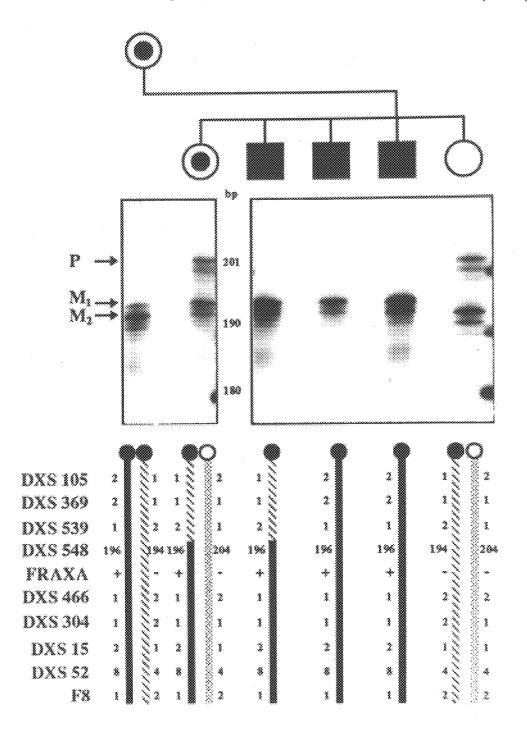


Figure 3

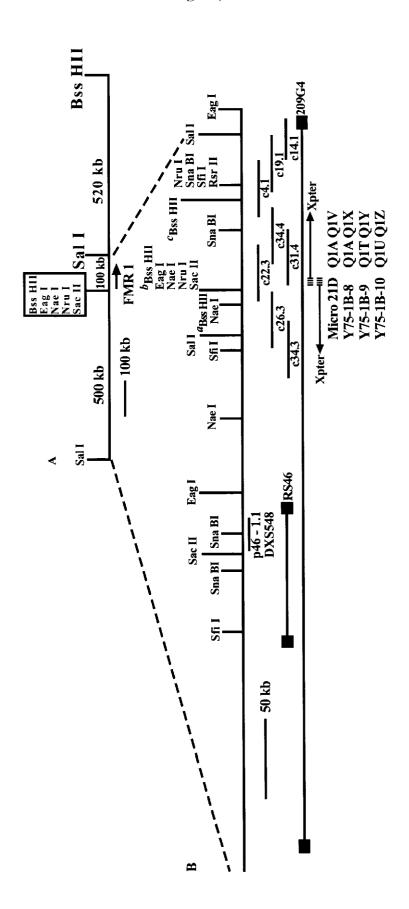


Figure 4

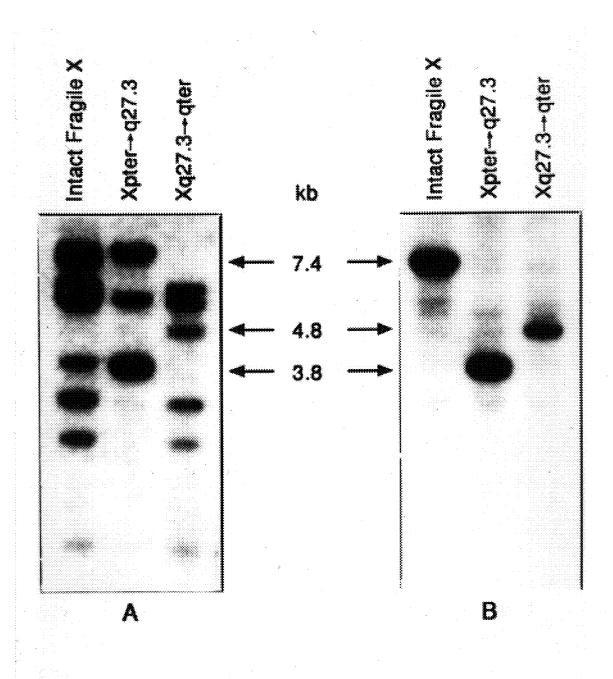
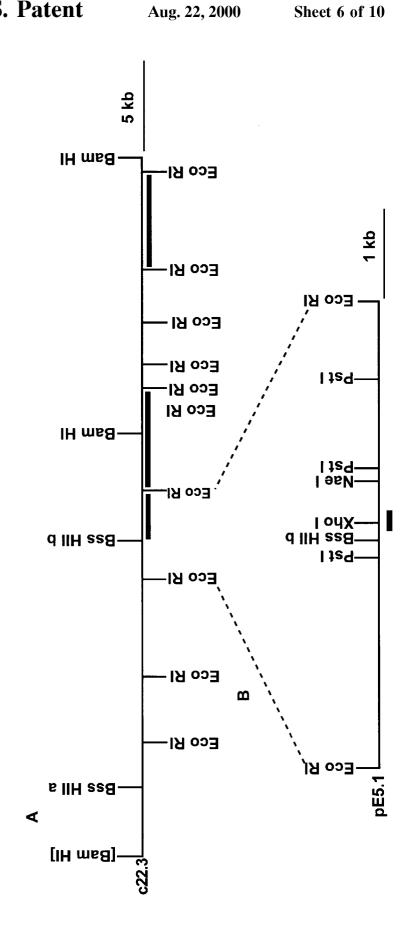


Figure 5



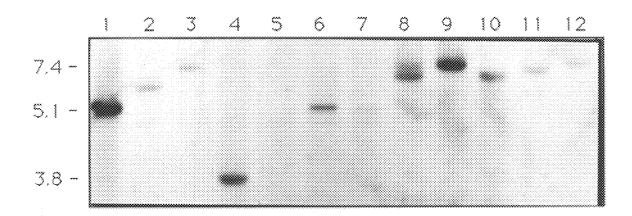


Figure 7

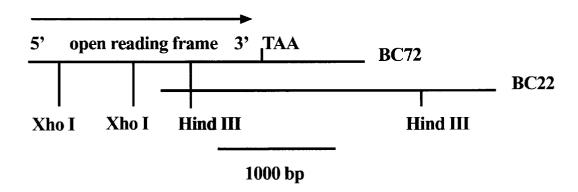
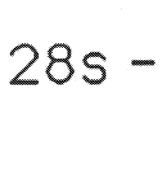


Figure 8

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Figure 9

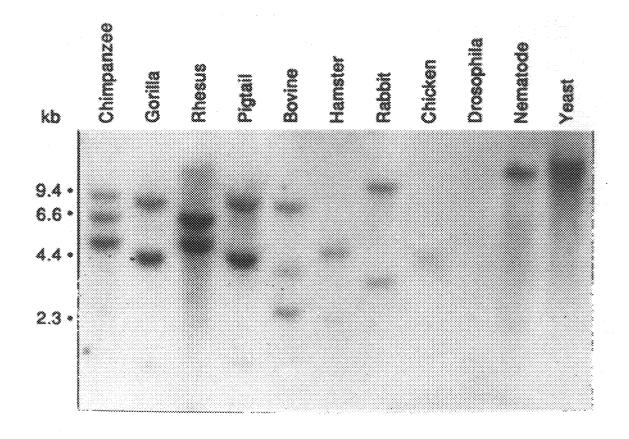


Figure 10