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Chromosomal localization of human homologs of the *Drosophila* heterochromatin protein 1 (*HP1*) gene

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Modifiers of position-effect variegation (PEV) and members of the *Polycomb*-group (*Pc*-group) genes encode proteins that are thought to modify chromatin, rendering it heritably changed in its expressibility (Gaunt and Singh 1990; Paro 1990). Isolation and sequencing of the *PC*-group namesake, *Polycomb* (*Pc*), has revealed a region of homology with a modifier of PEV known as heterochromatin protein 1 (HP1) (Paro and Hogness 1991). We have shown that the region of homology shared by HP1 and *Pc*, termed chromo box, can be used to detect homologous sequences in a wide range of animal and plant species (Singh et al. 1991). In addition, this conserved motif has been used to clone the first chromobox-containing genes from mouse (*M31* and *M32*) and human (*HSM1*). We have argued that the mammalian HP1-like genes might function as gene repressors in a manner similar to their fly homolog, perhaps by serving as components of heterochromatin.

Recently we have proposed a model of human X Chromosome (Chr) inactivation involving a process similar to that already described for PEV in *Drosophila* (Muscatelli et al. 1992). It was, therefore, of great interest to us to map the human homologs of the *Drosophila HP1* gene, to see whether they might be involved in this process. This communication describes the map position of autosomal copies of *HSM1* homologs by use of a combination of somatic cell hybrids and in situ hybridization.

At high stringency, six hybridizing bands could be seen in human genomic DNA restricted with *Eco*RI when *HSM1* was used as a probe (Fig. 1). When the stringency was lowered, additional bands were revealed (data not shown), suggesting that the gene family to which *HSM1* belongs is large, although there may be up to six genes with close homology. The chromosomal localization of these clone homologs was de-

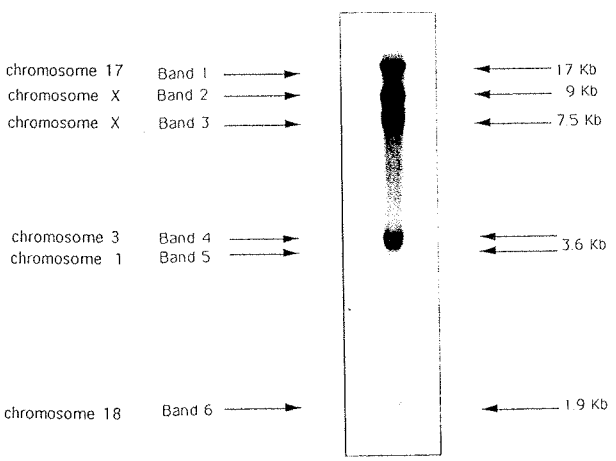

Fig. 1. Hybridization of human genomic DNA (10 μg) restricted with *Eco*RI with *HSM1* probe. Six hybridizing bands were detected after a final wash in 0.5 × standard sodium citrate at 65°C. These bands are respectively located on Chrs 17, X, X, 3, 1, and 18. Band number and molecular weight are indicated. The Southern blot was done according to standard procedures (Sambrook et al. 1989).

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Table 1. Chromosomal content of the panel of somatic cell hybrids.

	Chr																							
Hybrid	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	X	Y
867	60	–	–	–	+	–	–	–	–	–	–	–	+	+	–	–	–	+	+	–	–	–	–	–
854	–	+	–	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
423	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
860	–	–	15	–	+	+	–	–	–	15	–	–	–	–	–	–	–	–	45	–	+	–	–	–
803	–	–	–	+	+	–	–	+	–	–	15	–	–	–	–	–	–	–	–	–	–	+	+	–
909	–	–	–	–	D	+	–	+	–	–	–	–	–	+	–	–	–	–	–	–	–	–	+	–
1006	–	–	–	55	+	–	+	+	–	–	–	–	+	–	+	–	–	–	+	–	+	–	–	–
811	–	–	–	–	–	–	–	+	–	–	–	–	–	–	–	–	+	+	–	–	–	–	–	–
967	–	–	–	–	+	–	–	+	–	–	–	–	–	–	–	+	–	–	–	–	–	–	–	–
734	–	–	–	–	+	–	–	–	+	–	–	–	–	–	–	–	–	+	–	–	–	–	–	–
968	–	–	–	–	+	–	–	–	+	–	–	–	+	–	–	–	–	–	–	–	–	–	+	–
683	–	–	–	–	+	–	–	–	–	–	+	45	–	+	–	–	–	–	+	–	+	+	–	–
507	–	–	+	–	+	–	–	–	–	–	–	+	–	+	–	–	–	–	–	40	–	25	–	+
750	–	–	–	–	D	–	–	–	–	–	–	–	+	+	+	–	–	–	+	–	–	–	–	–
1099	+	–	–	–	D	–	–	–	–	–	–	–	+	–	–	–	–	–	+	–	+	+	–	–
324	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	+	–	–	–	–	–	–
940	–	–	–	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–	–	+	–	–	–	–
983	–	–	–	–	+	–	–	–	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–	–

D = deletion at p15.1–15.2. This panel of somatic cell hybrids was purchased from Bios Co. The numbers are the percentage of the cell population containing the noted chromosome. The chromosome content (+ for presence, – for absence in a hybrid) in the hybridization panel was quoted from the information from Bios Co.

termined with a panel of somatic cell hybrids. Using this panel (Tables 1 and 2), we found that band 1 localizes to Chr 17 (this result is in agreement with the localization of one of the mouse genes, used to screen the human library, to Chr 11, unpublished). Bands 2 and 3 were localized to the X Chr, band 4 to Chr 3, band 5 to Chr 1, and band 6 to Chr 18. With local somatic cell hybrids, band 1 was localized to 17q11–q21.

To confirm the mapping of these loci and provide a more precise regional localization, in situ hybrydization to human chromosomes (for technical references see Mattei et al. 1985) was performed with *HSM1*. Six hybridization peaks were reproducibly detectable (Fig. 2), and these were located on Chr 1 (10.2% of total silver grains), 3 (8.8%), 17 (7.9%), X (two loci have been detected representing 13.8% of total silver grains), and 18 (3.7%). More precisely, the respective locations of these six loci were:

Chr 1: 60.5% of the grains on this chromosome were mapped to the q32.1–q41 region with a maximum in the 1q32 band.

Chr 3: 59.5% of the grains were mapped to the q24–q26.1 region with a maximum in the 3q25 band.

Chr 17: 78.6% of grains were located in the q12–q21.3 region with a maximum in the 17q21 band.

Chr 18: 64.3% of the grains were located in the q21.1–q21.3 region with a maximum in the band 18q21.1.

Chr X: one peak represented 50.9% of the grains and was located in the p21.3–p22.2 region with a maximum in the p22.1 band. Another peak represented 30.9% of the grains and was located in the q11.1–q13 region with a maximum in the Xq12 band. These X Chr localizations have already been published (Reik et al. 1992), as well as the equivalent X-linked mouse gene (Hamvas et al. 1992).

In conclusion, six close human homologs of *HSM1* are found in the human genome, and their localization has been presented in this report. We do not know which of these loci corresponds to *HSM1*. The function of the protein products encoded by these genes is also not known, although we have suggested that they might be components of heterochromatin and therefore could act as gene repressors. We have also suggested that mutation in these genes may give rise to disease states (Singh et al. 1991), perhaps by aberrant activation of normally silent genes. Interestingly, the murine *posterior sex combs* gene, a member of the *Pc*-group of genes, has been shown to possess considerable sequence homology to the *bmi-1* oncogene (Brunk et al. 1991; Louhuizen et al. 1991).

Table 2. The chromosomal localization of *HSM1* homologs on the panel of somatic cell hybrids. Five μg of total human DNA, 5 μg of hamster DNA, and 8 μg of hybrid cell DNA has been digested with *Eco*RI and blotted on a nylon membrane (Bios Co). The blot was hybridized with the HSM1 insert (1.1 kb) as a probe. The presence (+) or absence (–) of one of the six human-specific *HSMN1* bands in somatic cell hybrids from the panel is indicated.

Hybrid	Band 1	Band 2	Band 3	Band 4	Band 5	Band 6
Human	+	+	+	+	+	+
Hamster	–	–	–	–	–	–
Hybrid 867	–	–	–	–	+	+
854	–	–	–	–	–	–
423	–	–	–	–	–	–
860	–	–	–	+	–	–
803	–	+	+	–	–	–
909	–	+	+	–	–	–
1006	–	–	–	–	–	–
811	+	–	–	–	–	+
967	–	–	–	–	–	–
734	–	–	–	–	–	+
968	–	+	+	–	–	–
683	–	–	–	–	–	–
507	–	–	–	+	–	–
750	–	–	–	–	–	–
1099	–	–	–	–	+	–
324	–	–	–	–	–	–
983	–	–	–	–	–	–

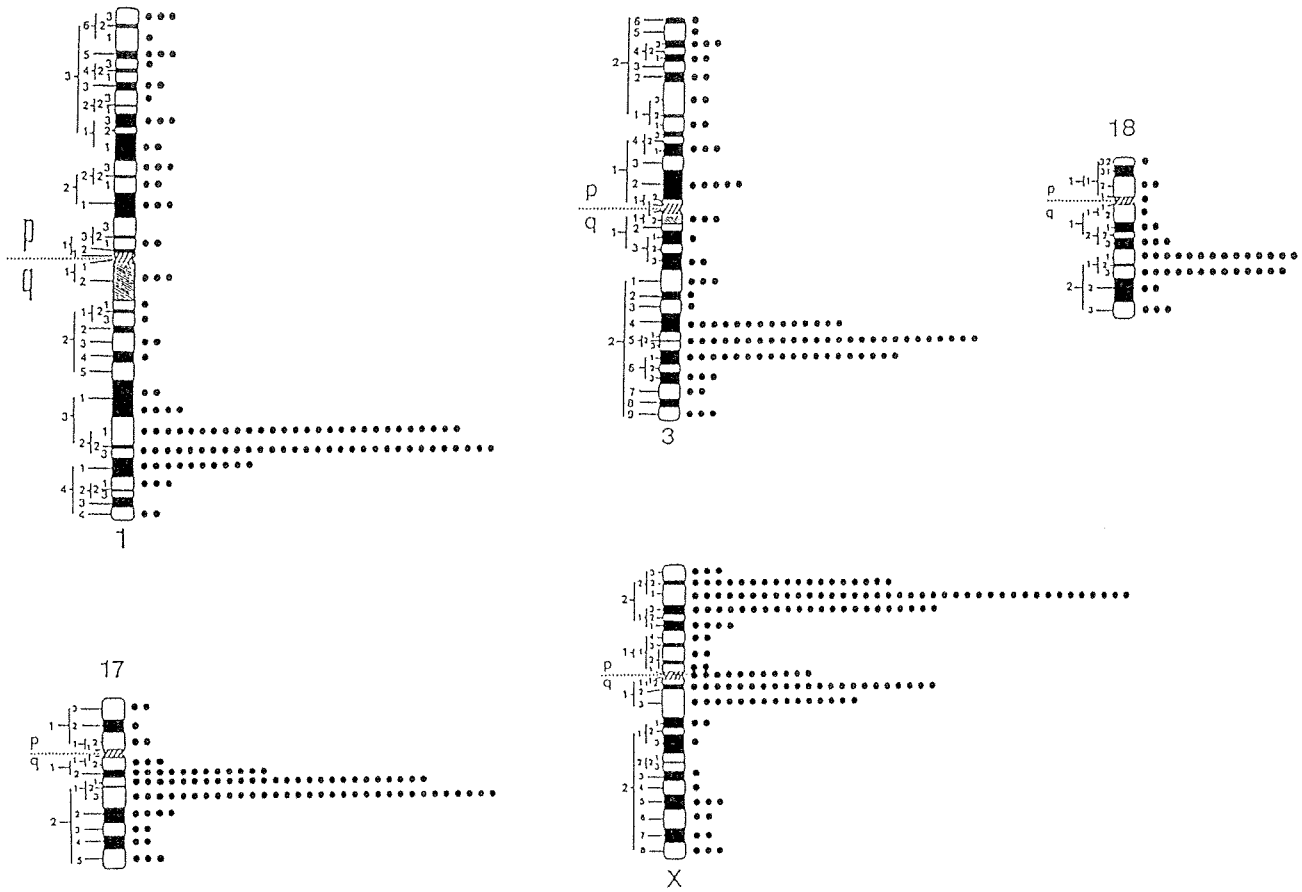

Fig. 2. Localization of *HSM1* to human chromosomes. Idiogram of the human G banded Chrs 1, 3, 17, 18, and X, illustrating the distribution of labeled sites. In situ hybridization (Mattei et al. 1985) was carried out on a chromosome preparation obtained from PHA-stimulated lymphocytes cultured for 72 h. Bromodeoxyuridine (60 μg/ml of medium) was added for the final 7 h of culture.

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