

Chromosomal localization of the transcription factor YY1 in the mouse and human

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YY1 is a ubiquitously distributed transcription factor belonging to the GLI-Krüppel class of zinc finger proteins. The YY1 cDNA was independently cloned in four different laboratories from human (Shi et al. 1991; Park and Atchison 1991) and mouse (Hariharan et al. 1991; Flanagan et al. 1992) tissues. Analysis of these cDNAs revealed that YY1 is highly conserved, showing 98.6% identity between the human and the mouse (Hariharan et al. 1991). Functionally, YY1 is an extremely versatile factor. It has been shown to be a negative regulator in some systems (Shi et al. 1991; Park and Atchison 1991; Lee et al. 1992; Bauknecht et al. 1992; Gumucio et al. 1992; Gualberto et al. 1992), and a positive regulator in others (Riggs et al. 1991; Hariharan et al. 1991). In some systems, the function of YY1 as an activator or a repressor is specified by the presence of other proteins (Shi et al. 1991). Finally, YY1 also binds to initiator elements and directs accurate basal transcription *in vitro* (Seto et al. 1991).

Previous studies had suggested the presence of a single *Yy1* gene in the murine genome (Hariharan et al. 1991). The cloning and characterization of this gene was recently described (Sáfrány and Perry 1993). In this report, we utilized an interspecific backcross provided by The Jackson Laboratory, (C57BL/6J × *M. spretus*) F₁ × *M. spretus*, to map the mouse *Yy1* gene.

A 396-bp human YY1 cDNA *SmaI-HindIII* fragment corresponding to amino acid residues 200–332 (Park and Atchison 1991) was used as the probe for Southern blot analysis. Within this region, there are only 17 nucleotide differences between human and mouse YY1 cDNAs (96% homology). According to the genomic structure of murine YY1 (Sáfrány and Perry 1993), this fragment should detect exons 2 and 3 in their entirety and portions of exons 1 and 4. The published restriction map of the mouse gene suggests that these exons should be present on four discrete genomic *HindIII* fragments. The fragment was labeled with the Random Primed DNA Labeling Kit (United States Biochemicals) and hybridized at 65°C to genomic DNA

blots. Restriction fragment length polymorphisms (RFLPs) between C57BL/6J and *M. spretus* were detected (data not shown). The *BglII* RFLP was selected for gene mapping (Fig. 1a). Genomic DNA samples from individual backcross progeny were then digested with *BglII* and hybridized with the same probe at 65°C. Analysis of the result unambiguously established the localization of the *Yy1* gene on mouse Chromosome (Chr) 12 between *D12Mit5* and *Igh-C* (*D12Mit8*). With these and additional animals, the intergenic distances (cM) were calculated as *Pmv-3*–(14 ± 4)–*D12Mit5*–(10 ± 4)–*Yy1*–(7 ± 3)–*Igh-C* (Fig. 1b).

Considering the ubiquitous expression of the YY1 protein and its apparent functional diversity, the exact phenotype of a YY1 mutant would be difficult to predict, and pleiotropic effects might be expected. Within the most likely interval for *Yy1* localization (D'Eustachio 1993), only one uncharacterized murine mutation, twitcher (*twi*), has been described. Biochemical and phenotypical evidence suggests that the product of the *twi* locus may be a secreted product (Yeager et al. 1984), possibly a galactosylceramidase (Kobayashi et al. 1980). It thus seems unlikely that YY1 is the product of the *twi* locus.

The region to which *Yy1* maps is part of an extensive linkage group (35 cM) containing 17 genes whose homologs map to human Chr 14q (D'Eustachio 1991, 1992, 1993). To confirm the localization of YY1 on human Chr 14, we used the same probe to hybridize *HindIII*-digested genomic DNA isolated from a panel of human–mouse and human–hamster somatic cell lines. Five hybridizing bands of 19, 6.5, 6, 3.5, and 2.5 kb were detected in human DNA. Of these, the 19-, 3.5-, and 2.5-kb bands were clearly localized on human Chr 14 (Fig. 2). These fragments probably represent the human homolog of the *Yy1* gene on murine Chr 12. If so, this confirms the predicted localization based on mouse–human chromosome homology. However, the definitive localization of the human YY1 gene cannot yet be determined. The strongly hybridizing 6.5-kb band was detected on human Chr 10. While this fragment may represent a duplicated YY1 gene or a YY1 pseudogene, the confirmation of this must await the cloning and characterization of the human YY1 gene. Finally, the more weakly hybridizing 6-kb band could not be mapped un-

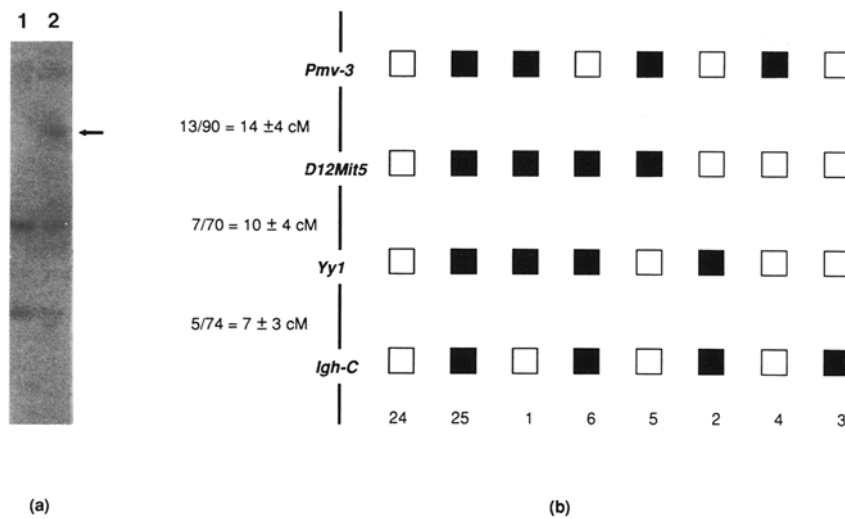


Fig. 1. (a) Photograph of part of the Southern blot used in mapping the *Yy1* gene. The arrow points to the *Bgl*III RFLP band specific to the C57BL/6J strain. Lane 1 shows the observed hybridization pattern of the *M. spretus* homozygote, and lane 2 shows that of the C57BL/6J-*M. spretus* heterozygote. (b) Haplotype distribution of 74 backcross progeny. Each column represents a chromosome haplotype. The number of animals observed with each haplotype is given below the column. Animals were scored at each locus either as heterozygous for the C57BL/6J and *M. spretus* alleles (■) or homozygous for the *M. spretus* alleles (□). The map distances in cM were calculated from the recombinant fraction observed for each individual (left).

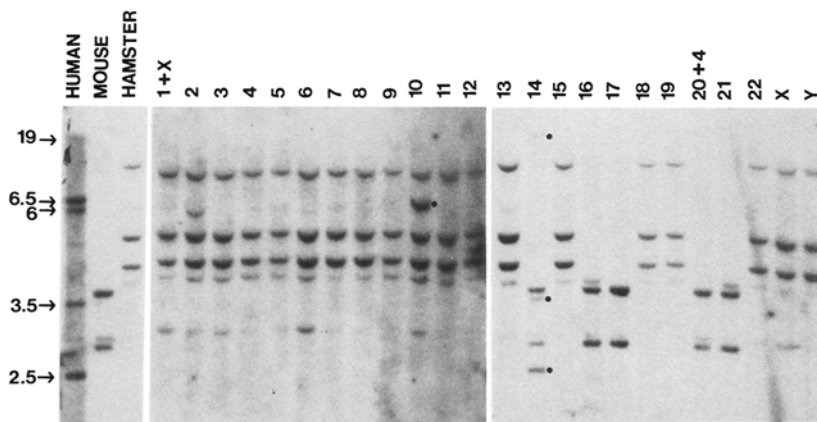


Fig. 2. Southern blot of DNA from human-mouse and human-hamster hybrids probed with the YY1 cDNA *Sma*I-*Hind*III fragment. The first three lanes represent genomic DNA from the human, mouse, and hamster digested with *Hind*III. Four fragments were detected in the mouse genomic digest, two of which were of <2.0 kb and are not shown. The sizes of the hybridizing fragments unique to human genomic DNA are indicated to the left of the photograph as 19, 6.5, 6, 3.5, and 2.5 kb. These results are similar to those published earlier (Hariharan et al. 1991). The specific human chromosome retained within each hybrid is indicated at the top of each lane. The presence of the 19-, 3.5-, and 2.5-kb bands in the hybrid containing human Chr 14 and the presence of the 6.5-kb band in the hybrid containing human Chr 10 are indicated by solid dots (●) beside these human-specific fragments.

ambiguously because it co-migrated with a restriction fragment from hamster DNA. These data thus suggest that the human genome may contain additional YY1 genes or pseudogenes.

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