Linkage Mapping of the Rat Msh2 DNA Mismatch Repair Gene on Chromosome 6

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Species: Rat (Rattus norvegicus)
Locus name: mutS (E. coli) homologue 2
Locus symbol: Msh2
Map position: D6Mit5: 0.5 cM - Msh2: 9.8 cM - D6Rat105
Method of mapping: Msh2 was mapped by genotyping male (ACI × BUF) F2 intercross rats (n=105) [1] with SSLP markers.

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Molecular reagents: Primer sequences used for SSLP analysis were 5′-GGCATATTAGTCTTTGCCTGAT-3′ (forward) and 5′-AAGAATGCAAGAGCAGAAGCTGA-3′ (reverse). PCR conditions were: 25 cycles of 94°C 0.5 min, 55°C 1 min and 72°C 1 min.

Allele detection: 130 bp in BUF/Nac and F344/Crj; 134 bp in DON and LEW; and 138 bp in ACI/N, BN, LEC/Crj, SD, TM/Kyo, WF, WKAH, WTC/Kyo and Zl/Kyo.

Previously identified homologues: Human MSH2 has been mapped to human chromosome (Chr) 2p16 [2, 4]. Mouse Msh2 has been cloned [10], and mapped to mouse Chr 17 [2].

Discussion: Mutations of the mismatch repair enzyme genes are known to play important roles in the development of human cancers with replication errors (RER+), which are characterized by the accumulation of microsatellite mutations [6]. One of the mismatch repair genes, hMSH2, is most often mutated in RER+ tumors [11], and its germline mutation is one of the major causes of hereditary non-polyposis colorectal cancers [2, 4]. The rat provides good models for colon carcinogenesis induced by various chemicals [3, 5, 8], and there is also a good model for genetics of high susceptibility to colon carcinogenesis [5]. Although the rat Msh2 gene was cloned [9], its chromosomal position has been unknown. A microsatellite polymorphism in an intronic region of the rat Msh2 gene, corresponding to human intron 5, was identified (Fig. 1) after searching polymorphisms in introns of the gene. With a mapping panel of 210 meiotic recombinations in ACI/N and BUF/Nac F2 intercross rats, it was mapped to a proximal part of the rat Chr 6 (Fig. 2). The information will serve to identify a candidate gene of interest as the Msh2 gene after linkage analyses, and to search for a loss of heterozygosity of the gene. The chromosomal synteny established by this study, human Chr 2p16, mouse Chr 17 (45.9 cM), and rat Chr 6, has not been reported [7], and will contribute to the construction of a precise comparative map among species.

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Fig. 1. SSLP analysis using F2 intercross of (ACI × BUF) F1 rats. Lanes 1–6: F2 intercross rats. Lanes 7, 8, and 9: ACI, BUF, and F1 rats, respectively.

Rat chromosome 6

![Diagram of Rat chromosome 6 with Msh2, D6Mit5, D6Rat105, D6Ncc6, D6Ncc5, D6Mgh7, D6Ncc18, D6Ncc4, D6Mlt2, D6Ncc9, D6Ncc10, D6Mgh4, D6Mgh3, and Ighe markers.]

Fig. 2. Chromosomal location of the rat Msh2 gene.

Acknowledgments

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References