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The Kell blood group locus is close to the cystic fibrosis locus on chromosome 7

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Summary. Linkage analysis confirmed the assignment of the Kell blood group locus to chromosome 7.

Introduction

Zelinski et al. (1991) recently showed that the Kell blood group locus (KEL) is tightly linked to the prolactin-inducible protein locus (PIP), which has been assigned to 7q32–q36. Based on this linkage they provisionally assigned KEL to chromosome 7. In this report we present the results of a linkage analysis between KEL and three DNA markers (D7S8, D7S23, D7S424) that are tightly linked to the cystic fibrosis locus, and confirm the assignment of KEL to 7q.

Materials and methods

Ninety-three individuals belonging to 12 two- and three-generation families were included in this analysis; they are part of a large collection of individuals that have been typed for many blood group and protein loci in our laboratory over the past 10 years. Kell phenotyping was performed on the red blood cells immediately upon arrival in the laboratory using anti K1, and DNA was extracted from the leukocytes. Genotypes for the D7S8 and D7S23 markers were determined using the polymerase chain reaction (PCR) followed by digestion with the restriction endonuclease *PstI*. The oligonucleotide sequences for amplification were obtained from Northrup et al. (1989) for D7S8 and Feldman et al. (1988) for D7S23. The microsatellite polymorphism at the D7S424 locus was analyzed using the primers given in Dean et al. (1990) and conditions described in Weber et al. (1991). Each of these markers has been shown to be tightly linked to the cystic fibrosis locus and they are assigned to the q31–q32 region of chromosome 7. Linkage analysis was performed using the MLINK and ILINK programs from the computer package LINKAGE (Lathrop et al. 1984). No recombinants were found between the three DNA markers, so haplotypes were constructed for analysis.

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Results and discussion

The results of the linkage analysis are shown in Table 1. The maximum lod score for sexes pooled is 3.76 at a recombination fraction of 0.105. Sex-specific estimates of the recombination fractions are 0.013 in males and 0.219 in females, with a joint maximum lod score of 4.58. The support intervals obtained by determining the recombination values corresponding to lod scores of 1 less than the maximum lod score are (0.0001, 0.18) and (0.06, 0.5) for the male and female recombination fractions, respectively.

This linkage analysis places KEL close to the cystic fibrosis locus, but it does not show if it is proximal or distal. However, Zelinski et al. (1991) found no recombinants between KEL and PIP, which is assigned to q32–q36. D7S8, D7S23, and D7S424 are in the q31–q32 region of chromosome 7, so KEL is probably distal to the cystic fibrosis locus. Of interest is the large difference in recombination fraction between males and females. A linkage map of chromosome 7 based on families from the CEPH reference panel (Lathrop et al. 1989) showed that recombination was significantly more frequent in females than in males, and the difference was particularly pronounced around q31.

Kell cDNA was recently cloned (Lee et al. 1991). Thus, the assignment to chromosome 7 by linkage analysis can now be confirmed using somatic cell hybrid mapping panels.

Table 1. Lod scores between the Kell blood group locus and D7S424/D7S8/D7S23

Sex	Recombination fraction						
	0.001	0.01	0.05	0.10	0.20	0.30	0.40
Male	3.76	4.12	4.03	3.70	2.89	1.95	0.96
Female	−3.82	−2.09	−0.57	0.06	0.44	0.39	0.17

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