Common Long Human Inversion Polymorphism on Chromosome 8*p*

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Abstract

In an analysis of human crossover interference, we identified apparent triple recombination events, in a short region on chromosome 8*p*, on the maternally-derived chromosomes in four individuals (two from each of two families). While this may have indicated an error in marker order, the inverted order was inconsistent with recombination events in other individuals. We were thus led to the hypothesis of an inversion polymorphism in the region, which was subsequently confirmed by fluorescent *in situ* hybridization (FISH). The inversion spans approximately 12 cM on the female genetic map and 2.5 – 5.3 Mb on the physical map. The allele frequency of the inverted order (D8S1130 telomeric; D8S351 centromeric) in 50 individuals of European ancestry was 21%. This is only the second known common, long inversion polymorphism in the human genome.

Keywords: CEPH; FISH; inversion; polymorphism

1 Introduction

Inversions in gene order along chromosomes have frequently been observed by comparing related species [14, 24, 25], including great apes [16, 21, 22, 29]. Human inversion mutations occur at a low, but detectable frequency. Paracentric (not involving the centromere) inversions that are large enough to be detectable by standard cytogenetic analysis occur at a frequency of 1 – 5 per 10,000 individuals [23]. The frequency of human submicroscopic inversions is unknown, although inversions have been identified as the cause of specific heritable disorders (see, for example, [1, 8, 15, 19, 20]). Chromosomal inversions are of particular clinical interest because recombination within the inverted region in heterozygotes can lead to segmental aneusomies and concomitant abnormalities.

The only well characterized common human inversion polymorphism is the 48 kb inversion of the Emery-Dreifuss muscular dystrophy and filamin genes on the X chromosome [26]. This inversion is present in populations of European descent at a frequency of about 18%. Page and colleagues also recently made a preliminary report of a potentially common 3 Mb inversion polymorphism on chromosome Y*p* flanked