Short report

Origin of the X chromosomes in a patient with the 49,XXXXY syndrome

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Recent progress in molecular genetics has facilitated the study of the parental origin of chromosome anomalies. In this report we present the results of X chromosome RFLP analysis undertaken on a 36 year old male with the 49,XXXXY syndrome and his parents.

The patient is the first child of healthy, unrelated parents who were aged 41 years (father) and 31 years (mother) at the time of his birth. Developmental delay and behavioural disturbance were apparent in early childhood and subsequently prompted admission to long term care at the age of 10 years. At recent examination the clinical findings were consistent with those of the 49,XXXXY syndrome and included microcephaly, upward slanting palpebral fissures, prognathism, bilateral fifth finger camptodactyly, marked limitation of pronation and supination, and small soft testes. Chromosome analysis from cultured lymphocytes showed the presence of a 49,XXXXY constitution in 45 (90%) out of 50 cells examined, with a 48,XXXY constitution in the remaining five (10%) cells. Parental chromosomes were normal.

X chromosome RFLP analysis using the pERT87-15 probe and *Xmn*I enzyme (figure a) showed a single 2.8 kb band in the father, the mother being homozygous for the more common allele comprising the 1.6 and 1.2 kb bands. The patient also showed only the 1.6 and 1.2 kb bands, both of which were much denser

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Autoradiographs of a Southern blot showing XmnI RFLPs detected by pERT87-15 (2.8 kb, 1.6+1.2 kb) (a) and pERT87-1 (8.7 kb, 7.5 kb) (b). M=mother, F=father, and P=patient with 49,XXXXY syndrome.

than in his mother. Using the pERT87-1 probe and *XmnI* enzyme (figure b), the mother was found to be heterozygous for the 8.7 kb and 7.5 kb RFLPs with both of these bands present in her son at approximately twice the dose.

In a few cases of the 49,XXXXY syndrome, it has been shown using Xg blood grouping that all of the X chromosomes were maternally derived.¹⁻³ Similarly, in the case now described, it is apparent using the pERT87-15 probe that all of the X chromosomes originate from the mother. Furthermore, use of the pERT87-1 probe indicates that both of the mother's alleles are present in her son and are equally represented. This would be consistent with either (1) non-disjunction of the mother's X chromosomes, with or without crossing over of the pERT87-1 alleles, in maternal meiosis I followed by non-disjunction of both X chromosomes either in maternal meiosis II or in the first postzygotic division, or (2) normal division of the X chromosomes in maternal meiosis I accompanied by recombination involving the pERT87-1 alleles, followed by non-disjunction of the X chromosome in maternal meiosis II with subsequent non-disjunction of both X chromosomes in the first postzygotic division.

The 48,XXXXY cell line probably originated from

a subsequent single non-disjunction, presumably anaphase lag. Although this mosaicism would be expected to produce a 5% difference in the density of the blots for the two X chromosome types, this differential is probably too small to be detected by the naked eye. Alternatively there could have been two or more non-disjunctions involving the loss of both X chromosome types as may occur, for example, in age related sex chromosome aneuploidy,⁴ although there was no evidence, such as premature centromeric division, to suggest that this phenomenon occurred in the culture from this patient.

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