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STRUCTURAL VARIATIONS AMONG THE CHROMOSOMES OF NORMAL HUMANS[1]

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DISCLAIMER

Introduction

There have been numerous reports of both normal and abnormal individuals with unusually large or unusually small Y chromosomes. Recently, it has become possible to identify unequivocally each human chromosome by its characteristic banding pattern with fluorescent dyes or with various treatments followed by staining with Giemsa (see: Paris Conference, 1971).

Most human Y chromosomes exhibit an intense fluorescence of a major portion of the long arm when stained with quinacrine(O'Riordan et al., 1971) or quinacrine mustard (Caspersson et al., 1971). The other G group chromosomes (21 and 22) exhibit easily identifiable fluorescence patterns. We report here the use of the fluorescence technique in a cytogenetic analysis of two individuals each exhibiting an unusually large G group chromosome, two others with a small G group chromosome, and, finally, a man and his unborn son with a very small G group chromosome. The results support the conclusion that a variety of polymorphisms of the long arm of the Y chromosome are not detrimental to life or to fertility. We suggest that such polymorphisms could be of use in studying isolated and inbred groups of people.

Materials and Methods

The original observations were made on standard air-dried slides stained with quinacrine dihydrochloride (see O'Riordan et al., 1971; Robinson and Buckton 1971). Quinacrine mustard staining (Caspersson et al., 1971) was employed for certain subsequent observations and for the photomicrography.

For the original observations, a Zeiss universal microscope equipped with a darkfield ultracondensor and 40 X apochromat and 100 X planachromat objectives (both with iris diaphragms) was used. A Leitz Ortholux microscope equipped with a Ploem illuminator and a 95 X planachromat objective was used for some observations and for photomicrography. Osram HBO 200 super high pressure mercury burners were used for illumination, and KP 490 interference filters were used as the excitation filters for both microscopes. Photographs were made on 35 mm. Plus X or Panatomic X film developed in HC 110, dilution B.

Fetal cells were obtained by amniocentesis and cultured in the manner standard in the second author's laboratory (Macintyre et al., 1971).

Results

In all six cases, chromosomes 21 and 22 were easily identified indicating that the unusual chromosome was the Y.

One phenotypically normal male had a large Y chromosome in which the long arm contained an extended region of highly fluorescent material.

The large Y chromosome of a second normal male also had an extended long arm. In this case the extended chromosome arm contained three seemingly discrete regions of strong fluorescence.

One phenotypically normal male had a small Y chromosome with a greatly reduced length of highly fluorescent material on the long arm. His son with the same karyotype was, however, not clinically normal.

In the remaining case, no brightly fluorescent spot characteristic of the Y chromosome was detected within the nucleus of the interphase fetal cells. In metaphase spreads two 21 chromosomes and two 22 chromosomes were easily identified by their characteristic fluorescence patterns. In the fifth small acrocentric chromosome the long arm was very short and completely lacked an intensely fluorescent region. There was no evidence of a translocation of brightly fluorescent material characteristic of the long arm of the Y to any other chromosome. The father and the fetus exhibited the same fluorescent karyotype. Therefore, as will be reported elsewhere (Macintyre and Rustad, in preparation), the pregnancy was not terminated, and a normal eight pound, one ounce male baby was born.

Discussion

Large Y chromosomes are not uncommon. In some instances, individuals with large Y chromosomes have been reported to have some physical and behavioral characteristics sometimes attributed to XYY males (e.g. unusual height and antisocial behavior, see: Harvey *et al.*, 1970; El-Alfi, 1970; Wahlström, 1971). Other males with large Y chromosomes seem entirely normal (e.g. Wahlström, 1971; Robinson and Buckton, 1971). Both males with large Y chromosomes in the present study looked phenotypically normal. Thus, it would appear that large Y chromosomes *per se* do not lead to phenotypic abnormalities.

Both males with large Y chromosomes had an excessive amount of brightly fluorescing material in the long arm. The fluorescent material in the Y chromosome of one of these men appeared as three discrete pieces. Three and even four discrete fluorescent bands have been reported in other large Y chromosomes (Wahlström, 1971).

The highly fluorescent region of the Y chromosome of phenotypically normal males can be small (e.g. Wahlström, 1971; Robinson and Buckton, 1971) or completely lacking (e.g. Borgaonkar and Hollander, 1971; Meisner and Inhorn, 1972). Thus, the two males with small fluorescent regions reported herein lend support to the concept that the strongly fluorescent region of the Y chromosome is not an essential component of the genetic material of the normal male. Indeed, no genetic function has been ever assigned to this region. However, we do not know why the son was abnormal.

Similarly, the complete absence of the fluorescent region of a normal father and his son found in the present study and in one other (Meisner and Inhorn, 1972) suggests that this material is not essential for normal development or for fertility. Since fluorescent material from the Y chromosome has been identified in translocations (e.g. Robinson and Buckton, 1971; Noel et al., 1971; Friedrich and Nielson, 1972), it appears unlikely that in the present case it was translocated and its normal staining properties were lost.

Differences in the lengths of fluorescent material appear to account for differences in lengths of Y chromosomes (Bobrow et al., 1971). The present study adds to a growing body of knowledge which indicates that seemingly normal males may have polymorphisms of the Y chromosomes in which either extra fluorescent material is present in the long arm or in which some or all of this material is lacking. However, since some individuals with unusual Y chromosomes are not normal, there is a clear need for statistically significant studies on the phenotypic variation and the fertility of these individuals. Nonetheless, variations in the amount of heterochromatin in the Y chromosome (as well as variations in the amount of centromeric heterochromatin, see: Craig-Holmes and Shaw, 1971) may prove to be important genetic markers for the study of isolated human groups.

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