Spatial relationship of human X and Y chromosomes at somatic metaphase

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SUMMARY A total of 592 cells was examined from 38 normal humans who had either small or very large Y chromosomes. Chromosome identification was based on the QFQ technique. The distance between the X and Y chromosome was measured from centromere to centromere. The spatial distance between X and Y was significantly smaller when the Y was small as compared to a very large Y ($p < 0.05$). The distance increased as the length of the Y chromosome increased and a significant correlation coefficient ($r = 0.58$) was found ($p < 0.05$). It is concluded that the length of the Y chromosome appears to play a major role in the non-random distribution of X and Y at somatic metaphase. The size and XY relationship in aneuploidy resulting from paternal non-disjunction and in patients with XXY and XYY should be investigated.

Information on the position of metaphase chromosomes may provide some important clues to the understanding of non-disjunction. It has been proposed that the distribution of human chromosomes at somatic metaphase is not random. For example, acrocentric chromosomes tend to lie closer to each other than would be expected by chance and the late replicating X chromosome tends to be near the periphery.¹ Furthermore, some suggest that the Y chromosome is located peripherally more often than other chromosomes, while others disagree with this notion.² This impression has prompted us to examine the distance between the X and Y chromosomes comparing small and large Y chromosomes. The object of this report is to determine whether the length of the Y chromosome affects its spatial relationship to the X chromosome at somatic metaphase.

Materials and methods

Thirty-eight normal males were selected from a project in progress because they had either a small Y with a Y/F index of 0.81 to 0.94 or a very large Y with a Y/F index of ≥ 1.23 . These males included East Indians, Caucasians, and American blacks. Lymphocytes from peripheral blood were cultured as usual and QFQ banding was performed on the slides.³ Cells were photographed on tri X film using a Zeiss photomicroscope II. Initially, 20 cells from each person were photographed. The method for

measuring the length of the Y chromosome has been described earlier.⁴ The distance from centromere to centromere between X and Y was measured in centimetres at somatic metaphase. The measurements were made directly by enlarging the negative to a final magnification of $\times 8500$. A total of 592 cells was included in the present study. Blind scoring was done with respect to the size of the Y. Only after completion of the study were the data compared.

In order to determine the 'functional relation' of one variable, for example, size of the Y chromosome, with another, for example, distance of X and Y, a regression coefficient analysis was performed. A test of significance of regression coefficient was also performed. In order to establish a causal relationship, correlation coefficient (r) analysis was also performed, that is, to examine the degree to which two variables vary together. A χ^2 test of significance was also performed to test the differences of two Y/F indices with distance.

Results and discussion

A total of 592 cells was examined from 38 subjects who had either a small or very large Y. The statistical parameters are classified in the table. The centromeric distance between X and Y was significantly smaller with small Ys compared to very large Ys ($p < 0.05$). The distance increased as the length of the Y chromosome increased and a significant correlation coefficient ($r = 0.58$) was found ($p < 0.05$) (figure). Therefore, a non-random distribution of sex chromosomes in human somatic metaphase is

TABLE Summary of statistical parameters of small and very large Y chromosomes.

Parameters		Race			Statistics
		Indian	Black	Caucasian	
Small Y	Y/F index (Y)	0.9380	0.8870	0.9083	$\bar{Y} = 0.9111$
	Distance (d)	6.80	4.95	4.55	$\bar{d} = 5.433$
	No of subjects (n)	1	2	9	$\Sigma n = 12$
	No of cells (C)	11	29	168	$\Sigma C = 208$
Very large Y	Y/F index (Y)	1.2982	1.3036	1.2549	$\bar{Y} = 1.2855$
	Distance (d)	6.82	6.48	5.70	$\bar{d} = 6.3333$
	No of subjects (n)	17	6	3	$\Sigma n = 26$
	No of cells (C)	231	94	59	$\Sigma C = 384$

$\Sigma \Sigma n = 38$.
 $\Sigma \Sigma C = 592$.

FIGURE Distribution of Y/F index with respect to distance (see text).

suggested. The long arm of the Y chromosome is heterochromatic because of length heteromorphisms. The longer Y resulted in duplication of constitutive heterochromatic material.⁵ The present observations suggest that constitutive heterochromatin might play an important role in the spatial relationship between the two sex chromosomes in man. Although such an approach has not been taken before, Wollenberg *et al*² strongly suggested a positive correlation between homologue chromosome (autosome) size and the distance from the centre of the metaphase. In addition, Schmidtke and Epplen⁶ have postulated that blocks of constitutive heterochromatin contribute to the non-random distribution of chromosomes at metaphase by preventing some of the pre-existing spatial relationships.⁷ Nevertheless, reports dealing with the ordered arrangement of chromosomes in man remain contradictory.^{8,9} So far only a strong association between acrocentric chromosomes owing to nucleolar organiser regions has been established. In addition, the peripheral position of the Barr body is well documented in the nucleolus of different tissues.¹⁰ It is tempting to speculate further that the position of the X might be fixed while the position of the Y might play an important role in determining the spatial relationship

between the X and Y. Based on the present observations, it is possible that so called 'junk DNA', which is the heterochromatic material on Yq, may have some fundamental biological effect in patients with sex aneuploidy (XXY or XYY etc). Since the spatial relationship may be influenced by the length of the Y chromosome, it is reasonable to suppose that Yq may be an important factor in non-disjunction in Klinefelter patients. A similar study of the size of the Y and XY relationships in aneuploidies where paternal non-disjunction has been established may be helpful in answering this question.

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