Short report

Assessment of Yqh translocations

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Abstract

Two initially presumed Yqh translocations, one to Xp and another to 21p, were assessed by conventional banding procedures, 5-azacytidine treatment, electron microscopy, and fluorescence in situ hybridisation. While the Yqh nature of the heterochromatic block from Xp was confirmed, this was not the case with the 21p+ variant. In conclusion, conventional banding techniques are insufficient to diagnose Y;G translocations.

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Constitutive heterochromatin located in the distal two-thirds of the long arm of the human

Y chromosome can be found translocated either to autosomes or to the sex chromosomes. In the case of autosomes, the short arms of the acrocentrics, mainly of chromosome 15, are reported to be the most frequently involved in the rearrangement, while the distal short arm of the X chromosome is the most common acceptor site in the case of the sex chromosomes.¹ The former cases appear to be clinically innocuous, being considered as normal variants, habitually familial. Nevertheless, the female carrier of an X;Y translocation is of short stature as a consequence of partial monosomy of the distal Xp which is lost in the der(X), while the male carrier is partially nullisomic for the deleted segment resulting in mental retardation, infertility, and possible mendelian diseases.¹

Assessment of an X;Y translocation involving the Yqh region (A-E) and a chromosome 21 variant with greatly enlarged satellite region (F-K). A and F: quinacrine staining; B and G: C banding. A heterochromatic block is evident in Xp and 21p. C and H: G banding. 5-azaC treatment results in condensation inhibition of the Xp heterochromatin while that of 21p is not undercondensed. E and K: Electron micrographs of whole mounted chromosomes. After 5-azaC treatment Xp heterochromatin is clearly less folded, while 21p maintains a highly packed block of chromatin bodies connected to the short arms by a stalk of less dense longitudinal fibres. L: Normal small human acrocentric chromosome. I: NOR silver staining. D and J: FISH with a DYZ1 locus probe. The undercondensed Xp heterochromatin is highlighted while 21p is not labelled.

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We have assessed two initially presumed Yqh translocations, one to Xp and another to 21p, by several procedures including 5-azacytidine (5-azaC) treatment, electron microscopy, and fluorescence in situ hybridisation (FISH). C banding obtained using either Ba(OH)₂ or in situ digestion with *Alu*I showed intense heterochromatic blocks in both Xp and 21p, confirming previous findings with Q banding (figure A,B and F,G).

5-azaC treatment (3.5×10^{-7} mol/l) during the last seven hours of lymphocyte culture induces a selective condensation inhibition of the constitutive heterochromatin of human chromosomes 1, 9, 15, 16, and Yq.² When this base analogue was used, it induced a clear undercondensation in the heterochromatin present in Xp, while condensation behaviour was not modified in distal 21p (figure C and H). Despite possible limitations in clarification of the chromatin structure, this fact was confidently confirmed through the high resolution achieved by electron microscopy (figure E and K) which showed a highly packed block of chromatin fibres at 21p instead of the typical small satellite structure. A stalk appeared adjacent to this heterochromatic block (figure K) (compare with the normal short acrocentric chromosome shown in the figure L). This finding was in accordance with Ag-NOR staining, which detected previous transcriptional activity of ribosomal cistrons of this chromosome in 85% of mitoses (figure I). This frequency was similar to that exhibited by the rest of the acrocentrics. NORs appear clearly located below the giant satellites, at the stalk level (figure I). Nevertheless, this chromosome was involved in satellite associations with acrocentrics in only 4.7% of mitoses (figure H and J), a significantly lower proportion than that shown by the normal 21 homologue (20.8%) (analysed in 250 mitoses). Although the heterochromatic block of this chromosome 21 variant does not affect the NOR expression, it could possibly interfere with its capacity to participate in the formation of a common nucleolus in interphase, thus showing a very low frequency of satellite associations in metaphase.³

Finally, when FISH was performed using a specific alphoid probe for the centromere of the Y chromosome (DYZ3 locus) no hybridisation

signals were detected in either chromosome, as expected. Otherwise, the classical satellite probe (DYZ1 locus) which delineates the Yqh region, mainly in the proximal region, hybridised on the Xp undercondensed heterochromatin (figure D), while its hybridisation signal was absent in 21p (figure J). This result illustrates the value of FISH as a routine part of chromosome diagnosis.

Haaf *et al.*⁴ summarised studies where the presence of human Y specific sequences was assessed in Dph+ and Gph+ chromosomes. All variant D chromosomes were indeed Y; acrocentric translocations. Nevertheless, only one chromosome 22 variant of six published, including their own case, contained Y heterochromatic sequences. In conclusion, the majority of the previously described Y;22 translocations are questionable. To our knowledge, no chromosome 21 variants have been analysed until this report. Despite only 16 presumed cases of Y;acrocentric translocations assessed for the presence of Yqh sequences, it seems likely that while most Dph+ variants represent true Yqh translocation products, most of Gph+ variants are probably not derived from the Y chromosome. In the case of the chromosome 22 variant described by Haaf *et al.*,⁴ the heterochromatin present at 22p was undercondensed after berenil treatment, which also undercondenses Yq heterochromatin. However, 5-azaC was not effective in inducing condensation inhibition in our chromosome 21 variant. This fact could reflect heterogeneity in the origin and nature of this heterochromatic material. Overall, our results support and extend the statement of Haaf *et al.*⁴ that conventional banding analyses are insufficient to diagnose Y;G translocations.

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