

LETTER

Meiotic segregation analysis by FISH investigations in sperm and spermatocytes of translocation heterozygotes

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It has been repeatedly claimed that in translocation heterozygotes information on meiotic analysis may be obtained via sperm investigations, either by karyotyping (for reviews see Martin,¹ Estop²) or FISH of sperm nuclei. This is exemplified by the recent paper³ in this journal entitled 'The meiotic segregation pattern of a

reciprocal translocation t(10;12)(q26.1;p 13.3) by fluorescence *in situ* hybridization sperm analysis', where it is stated that 'adjacent I segregation predominates in many translocation carriers'. This is not a valid statement due to the limitations of FISH of sperm for obtaining information on meiotic segregation patterns of reciprocal translocations. Firstly, only data on adjacent II and the infrequent categories of 3:1 and 4:0 segregants can be identified, if using centromeric probes. Further, even if telomeric probes are used, it is

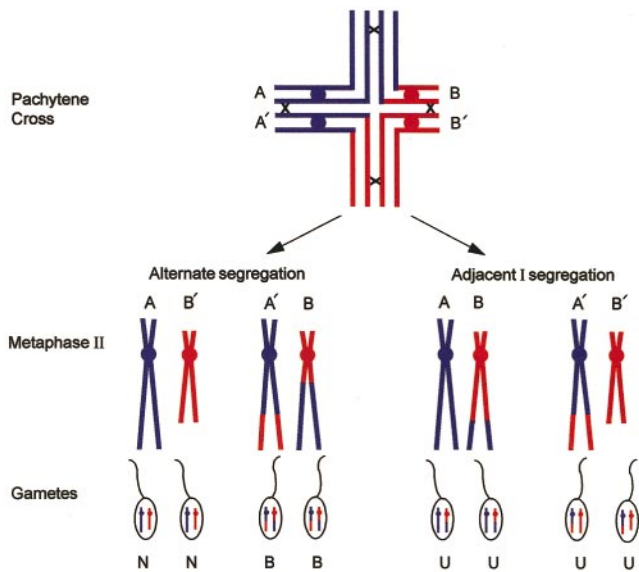


Figure 1(a) Outcome of first meiotic segregation with no interstitial chiasmata. Alternate segregation produces 50% balanced (B) products (sperm), whereas Adjacent I segregation produces 100% unbalanced (U) products. Note: using centromeric probes alone will not distinguish between these products.

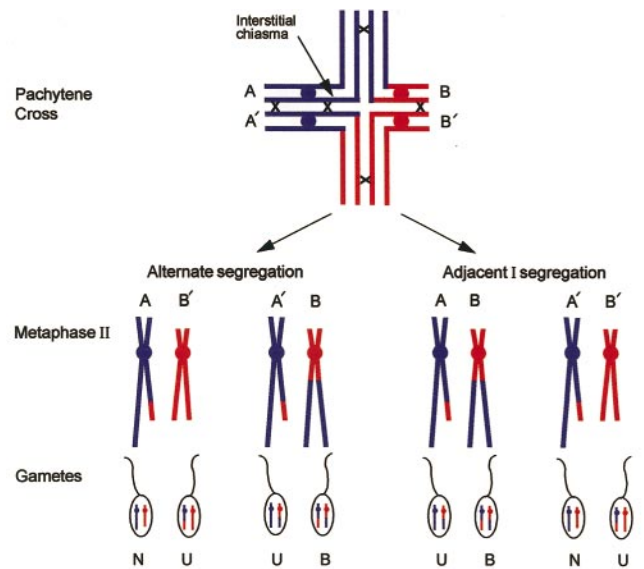


Figure 1(b) Outcome of first meiotic segregation with interstitial chiasma. Alternate segregation produces 25% normal, 25% unbalanced and 50% unbalanced gametes. Adjacent I segregation produces the same frequencies. Note: even if probes are used distal to the breakpoint, it is not possible to determine their origin, either Alternate or Adjacent I category of segregation.

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still not possible to tell whether the gametes were derived from adjacent I or alternate segregations, where this is complicated by an interstitial chiasma.

It is a well known fact, and is clearly stated in many publications, including textbooks,^{4,5} that whenever an interstitial chiasma is present, asymmetric dyads are produced at anaphase I. These could be derived from either alternate or adjacent I segregations. Thus anaphase II products of these segregations will be 25% normal, 25% balanced and 50% unbalanced. This is in contrast to the situation without an interstitial chiasma, as illustrated in Figure 1.

Using FISH on testicular biopsies, we have examined four reciprocal translocation carriers.^{4,6,7} Analysis of metaphase I demonstrated that the reciprocal translocation chromosomes regularly form quadrivalents as is generally the case, even when the translocated segments are very small. Most importantly, there is a high frequency of a single chiasma within the interstitial segments. This was found in no less than 48% for the t(1;11), 31% for the t(15;20), 95% for the t(11;22) and 100% for the t(9;21) translocation heterozygotes.^{4,6,7} These frequencies are substantially increased in comparison to chiasma formation within these segments in the normal male.⁸ Adequate information on the occurrence of chiasmata within the interstitial segments can only be obtained by meiotic studies of the respective translocation carriers. Using FISH it has been possible to identify the interstitial chiasma frequency and resultant asymmetric dyads. This analysis thus differentiates between the three categories: (1) alternate, (2)

adjacent I and (3) alternate/adjacent I. However, it is important to note that even FISH meiotic studies do not allow us to state whether alternate or adjacent I segregation predominates in male translocation carriers!

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