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Satellite Associations of D Group Chromosomes in Translocation Carriers

Y. NAKAGOME and A. D. BLOOM

From the Department of Human Genetics, University of Michigan Medical School, Ann Arbor, Michigan, U.S.A.

Satellite association has been postulated to increase the risk of either non-disjunction or translocation between acrocentric chromosomes (Ferguson-Smith and Handmaker, 1961; Ohno *et al.*, 1961; Ferguson-Smith, 1964). Further, an increased incidence of satellite association has been observed in families with translocation and multiple cases of mosaicism (Zellweger, Abbo, and Cuany, 1966; Abbo, Zellweger, and Cuany, 1966).

Recently, Nakagome (1969) and Shaw, Craig, and Ricciuti (1969) showed that, in normal subjects, the members of the three pairs of D group chromosomes were randomly involved in satellite associations. However, these findings do not preclude the possibility that there are non-random patterns of associations in people who are 'predisposed' to translocation or non-disjunction.

Materials and Methods

Two carriers with t(14qGq) from one family and two carriers with t(13q14q) from another family were studied. Both translocations were of the centric-fusion type.

The peripheral blood culture and autoradiography techniques used are described elsewhere (Nakagome, 1969). During the last five hours of the standard leucocyte culture (72 hours), cells were treated with ^{3}H-thymidine. The final concentration was 0·5 μCi/ml. and the specific activity was 2Ci/mmole. The criteria for satellite association were either the presence of visible connexions between satellited ends of acrocentrics or the presence of acrocentrics within a distance of one chromatid width of each other, with orientation towards a common point by the satellited ends. Only cells with satellite associations involving the D chromosomes were scored. After autoradiography, cells were classified as type A, B, or C according to their labelling patterns. When each chromosome of the D group was typically labelled, cells were classified as type A. When one (in 13q14q cases) or two (in 14qGq cases) No. 13's were definitely identifiable and there were difficulties in the identification of some or all of the other D group chromosomes, cells were classified as type B. When both No. 15's were identified, cells were classified as type C. In type B cells, involvement of the identified No. 13's in satellite associations was compared with the rest of the D group chromosomes. Type C cells were used to compare the No. 15's with the other D chromosomes. Cells with other labelling patterns, such as only one identifiable No. 15, were not included in the series to avoid bias.

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Results

The results from the two cases of t(14qGq) carriers are summarized in Table I. Since the data obtained from these two cases were similar, the results were here combined. The D chromosomes of type A cells were involved in satellite associations 63 times (25 in one case, 38 in the other). The excess involvement of No. 15 above the expected value, and the lesser involvement of No. 13 are striking (χ^2(d.f. = 2) = 9·42, $p < 0·01$). In 52 type B cells (29 in one case, 23 in the other) and in the combined B plus A cells, a conspicuous decrease of No. 13's and an increase of the other two members of the D chromosomes in satellite associations were observed ($p < 0·005$ and $p < 0·001$, respectively). Type B and A cells were combined because these types of cells were the most common and presumably provided the best data available for comparison of the frequency of No. 13 associations, with that of the other D group chromosomes. In 74 type C cells (33 in one case, 41 in the other), the results were not significant (χ^2(d.f. = 1) = 2·30 $p < 0·2$); however, there was a slight increase of No. 15's. When both type C and A cells were combined, χ^2 increased to 10·07 (d.f. = 1, $p < 0·005$) and an excess of No. 15 was observed.

The results obtained in two cases of t(13q14q) are shown in Table II. The results are in agreement with the concept of random involvement in satellite associations of each of four members of the D group chromosomes.

Discussion

D group chromosomes seem not to be randomly

TABLE I

NUMBER OF D GROUP CHROMOSOMES INVOLVED IN SATELLITE ASSOCIATIONS IN 2 CASES WITH t(14qGq) TRANSLOCATION

	No. of D Group Chromosomes Associated									
	Type A Cells		Type B Cells		Type A and B Combined		Type C Cells		Type C and A Combined	
	Obs.	Exp.*	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
No. 13	16	25·2								
No. 14	10	12·6								
No. 15	37	25·2								
No. 13			11	20·8	27	46·0				
Nos. 14 and/or 15			41	31·2	88	69·0				
Nos. 13 and/or 14							38	44·4	64	82·2
No. 15							36	29·6	73	54·8
Total	63	63·0	52	52·0	115	115·0	74	74·0	137	137·0
χ^2	9·42		7·96		13·08		2·30		10·07	
d.f.	2		1		1		1		1	
p <	0·01		0·005		0·001		0·2		0·005	

* The expected numbers are calculated on the assumption that each member of the D group chromosomes has the same probability of being involved in satellite associations.

TABLE II

NUMBER OF D GROUP CHROMOSOMES INVOLVED IN SATELLITE ASSOCIATIONS IN 2 CASES WITH t(13q14q) TRANSLOCATION

	No. of D Group Chromosomes Associated									
	Type A Cells		Type B Cells		Type A and B Combined		Type C Cells		Type C and A Combined	
	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.	Obs.	Exp.
No. 13	19	19·25								
No. 14	13	19·25								
No. 15	45	38·50								
No. 13			16	15·25	35	34·50				
Nos. 14 and/or 15			45	45·75	103	103·50				
Nos. 13 and/or 14							23	23·50	55	62·00
No. 15							24	23·50	69	62·00
Total	77	77·00	61	61·00	138	138·00	47	47·00	124	124·00
χ^2	3·13		0·05		0·01		0·02		1·58	
d.f.	2		1		1		1		1	
p <	0·25		0·90		0·95		0·90		0·25	

involved in centric fusion type translocations. Hecht *et al.* (1968) reviewed 13 cases of t(DqGq) from published reports, and added 20 cases of their own. 30 of these cases were translocations between a G and a No. 14, and the remaining 3 were between a G and a No. 15. In at least 13 different families with t(DqDq) (centric-fusion type), the D chromosomes involved were shown to be a No. 13 and a No. 14 (Yunis *et al.*, 1964; Dekaban, 1966; Giannelli and Howlett, 1966; Rowley *et al.*, 1967; Bloom and Gerald, 1967; Krmpotic, Ramanathan, and Grossman, 1968; Kohno and Makino, 1969; Palmer, Conneally, and Christian, 1969; Nakagome, 1969). There have been only 3 cases with other combinations (Giannelli, 1965; Higurashi *et al.*, 1967; Lucas, 1969). On the other hand, D group chromosomes do seem to be randomly involved in reciprocal, and non-centric-fusion type, translocations. According to Bloom and Gerald (1968), out of 6 reported cases of reciprocal translocations, 3 involved No. 13, 1 a No. 14, and 2 a No. 15.

It seems reasonable to assume that there are control mechanisms that affect the satellited end of D chromosomes, and thereby determine which of the individual chromosomes are involved in centric-fusion type rearrangements. One possible explanation, suggested by Hecht *et al.* (1968), is that the area close to the centromere of No. 14 replicates later than the same area of Nos. 13 and 15, presumably representing differences in molecular organization and predisposing the area to breakage. While this may explain the excess of t(14qGq), it

does not account for the observed excess of t(13q14q) and the absence of t(14q15q).

Another possible explanation is the non-random entry of D chromosomes into satellite associations. As shown in earlier studies (Nakagome, 1969; Shaw *et al.*, 1969), and as confirmed by the present study on 2 cases with t(13q14q), satellite association is generally random. However, in some specific instances it may be non-random, as suggested by our 2 cases with t(14qGq). In these 2 cases, No. 13 was found in satellite associations much less frequently than expected, and No. 15 was seen much more frequently. The D chromosome involved in the translocation was a No. 14, and yet the one most frequently involved in satellite associations was not a No. 14. This non-randomness may be limited to these particular individuals; or, alternatively, it may be found in many other individuals, particularly within those families with certain types of chromosomal rearrangements or families with multiple cases of aneuploidy involving the acrocentric chromosomes. In any event, this 'non-randomness' warrants further studies of satellite associations in individuals who are 'predisposed' to chromosomal aberrations.

Summary

Cultured lymphocytes from two cases of t(14qGq) and two cases with t(13q14q) were labelled with ^{3}H-thymidine. D group chromosomes involved in satellite associations were identified based on their labelling patterns. In 2 cases with t(14qGq), D chromosomes were not randomly involved in satellite associations. An excess of No. 15's and a deficiency of involvement of the No. 13's were observed. The results were highly significant. In 2 cases with t(13q14q), the D chromosomes associated randomly.

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