TWO LEVELS OF ASSOCIATIVE POTENTIAL OF ACROCENTRIC CHROMOSOMES IN TWO CHROMOSOMAL ASSOCIATIONS OF HUMAN LYMPHOCYTES

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There are as yet no direct criteria to characterize the associative potential of each acrocentric chromosome. The frequencies of the different types of associations indicate the character of the quantitative distribution of associations and give an indirect idea of the associative potential of the participating chromosomes. Attempts are being made to detect definite relationships between associative potentials and certain morphological features of chromosomes. The size of the satellites and the dimensions of the nucleolar organizers are used as such features, but comparison of satellite size and dimensions of nucleolar organizers with frequencies of participation of chromosomes in associations does not reveal a high degree of correlation [3-10].

The main difficulties arising during correlation analysis occur during determination of the size of satellites and the length of nucleolar organizers, and also during the identification of satellite associations themselves; dimensions and lengths are determined by eye, and this significantly affects the reliability of the calculations, but a mistake during the identification of associations on the basis of mutual orientation introduces quite considerable additional errors. The use of stains to detect fibrillary connections between satellites in chromosomes participating in associations has enabled the associative potential of acrocentric chromsomes to be studied in greater depth.

This paper gives the results of a study of the associative potential of acrocentric chromosomes in two chromosomal associations of lymphocytes from healthy blood donors.

EXPERIMENTAL METHOD

Chromosomal preparations were obtained in the usual way from a 72-h culture of peripheral blood from 10 healthy donors. These were stained for G bands, and on the basis of its results pairs of acrocentrics were identified and their spatial arrangement in the metaphase plate was drawn. Fibrillary connections between satellites of acrocentric chromosomes participating in associations were detected by staining with ammoniacal silver. The metaphases to be studied were localized once again on the vernier scale and chromosomes participating in associations were determined from connections between satellites. A group of chromosomes linked by intersatellite connections was taken as an association regardless of their mutual orientations or distance from one another. Associations of the DD and GG types were divided into those formed by homologous and nonhomologous chromosomes, whereas associations of chromosomes of different groups of the DG type were subdivided, depending on the participating G chromosome, into $A_{21}\cdot A_{13}$, $A_{21}\cdot A_{14}$, $A_{21}\cdot A_{15}$, $A_{22}\cdot A_{13}$, $A_{22}\cdot A_{14}$, and A_{22}. The frequencies of all 15 types of two-chromosome associations were determined and from them the corresponding relative frequencies were calculated [1, 2].

EXPERIMENTAL RESULTS

The best objects for the study of associative potential in acrocentric chromosomes consists of associations in which only two chromosomes interact and there are no possible "disturbing" influences of other chromosomes. Among them, associations formed by chromosomes of the same group – DD and GG – are particularly interesting. There are three possible variants of associations among those of the DD type, con-

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TABLE 1. Calculation of Associative Potentials of Acrocentric Chromosomes from Frequencies of Two-Homolog Associations and Testing by the χ^2 Method the Hypothesis of Existence of a Second Level of Associative Potential in Acrocentrics in Assocations of Nonhomologous Chromosomes Belonging to Different Groups

Type of associations	Subclasses of associations	Empirical frequencies	Associative potential of chromosomes	Product of associative potentials of corresponding chromosomes	Ratio of empirical to theoretical frequencies	Coefficient of associative potential	Theoretical frequencies allowing for coefficient of potential	Frequencies	
								empirical	theoretical
DD: Homologs (0,0740)	$A_{15}\cdot A_{15}$	0,0127	0,113	—	—	—	—	6	6
	$A_{13}\cdot A_{13}$	0,0296	0,172	—	—	—	—	14	14
	$A_{14}\cdot A_{14}$	0,0317	0,178	—	—	—	—	15	15
Nonhomologs (0,2685)	$A_{13}\cdot A_{15}$	0,0698	—	0,0194	3,5979	1,90	0,0831	33	38,56
	$A_{14}\cdot A_{15}$	0,0888	—	0,0201	4,4179	2,10	0,0861	42	39,91
	$A_{13}\cdot A_{14}$	0,1100	—	0,0306	3,5948	1,89	0,1311	52	60,75
DG: 21-D (0,2644)	$A_{13}\cdot A_{21}$	0,1036	—	0,0237	4,3713	2,09	0,1016	49	47,09
	$A_{14}\cdot A_{21}$	0,0930	—	0,0246	3,7805	1,94	0,1054	44	48,74
	$A_{15}\cdot A_{21}$	0,0677	—	0,0156	4,3397	2,08	0,0668	32	30,94
22-D (0,2622)	$A_{15}\cdot A_{22}$	0,0909	—	0,0147	6,1837	2,49	0,0629	43	29,15
	$A_{13}\cdot A_{22}$	0,0888	—	0,0224	3,9643	1,99	0,0959	42	44,36
	$A_{14}\cdot A_{22}$	0,0824	—	0,0231	3,5671	1,89	0,0990	39	45,91
GG: Nonhomologs	$A_{21}\cdot A_{22}$	0,0951	—	0,0179	5,3128	2,30	0,0767	45	35,59
Homologs (0,0359)	$A_{21}\cdot A_{21}$	0,0190	0,138	—	—	—	—	9	9
	$A_{22}\cdot A_{22}$	0,0169	0,130	—	—	—	—	8	8
Total . . .	15	1,0000	—	—	4,3130	2,07	—	473	473,00

Legend. Frequency of associations given in parentheses. χ^2 observed 12.96, χ^2 critical 23.7.

sisting of homologous chromosomes ($A_{13}\cdot A_{13}$, $A_{14}\cdot A_{14}$, $A_{15}\cdot A_{15}$) and the same number of variants consisting of nonhomologous chromosomes ($A_{13}\cdot A_{14}$, $A_{13}\cdot A_{15}$, and $A_{14}\cdot A_{15}$). In associations of the GG type there are two possible variants from homologs ($A_{21}\cdot A_{21}$, $A_{22}\cdot A_{22}$) and one from nonhomologs ($A_{21}\cdot A_{22}$).

Given the strict constancy of the number of acrocentric chromosomes in the cell, the theoretical frequencies of associations from homologous and nonhomologous chromosomes in the D and G group ought to be roughly the same in the cell population. However, empirical data do not agree with theoretical predictions (Table 1). Frequencies of associations of two G homologs (0.0359) were 2.6 times lower than frequencies of associations of two nonhomologous G chromosomes (0.0951). This means that associations of two G homologs are formed 2.6 times less frequently than associations of two G nonhomologs.

Comparison of frequencies of associations of homologous (0.0740) and nonhomologous (0.2685) D chromosomes showed a much greater (3.6) decrease in frequencies of associations of two D homologs. The question arises why, during interaction of two D or two G homologs with one another, several times fewer associations are formed than during interaction between two nonhomologous chromosomes of the same groups. Given quantitative constancy of D and G chromosomes in the cell, the fact that associations of nonhomologous chromosomes are 2.5 and 3.5 times more frequent may be due to a change in their associative potential.

The associative potentials in acrocentric chromosomes were analyzed in a sample of 473 two-chromosome associations. Other conditions being the same, a larger number of associations was formed by acrocentrics with higher associative potential. If the frequency of associations depends on associative potential of the chromosomes, it can be used for quantitative assessments. In that case, the associative potential is expressed in a concrete manner through empirical frequencies and, consequently, the frequencies of two-chromosome associations in which the acrocentric chromosomes participate.

Any two-chromosome association was regarded as the combined performance of two independent events A_i and A_j, where A_i (A_j) represents an event consisting of the entry of chromosome i (j) into an association. The product $A_i\cdot A_j$ when $i \neq j$ is an event leading to the formation of an association of nonhomologous acrocentrics belonging to different groups. The product $A_i\cdot A_j$ when $i = j$ is an event consisting of the formation of associations from a pair of homologous chromosomes. Other conditions being the same, homologous chromosomes in associations will possess similar and, perhaps, equal associative potential. Taking this and the frequencies of formation of associations by homologs into account, their associative potentials were calculated. If they are designated a_{ij}, where i, j = chromosomes 13, 14, 15, 21, and 22, the probability of appearance of an association of two homologs ($i = j$) will be given by $a_i a_j = a_i^2$, and the associative potentials of each homolog will be $\sqrt{a_i^2}$.

If each acrocentric chromosome has its characteristic associative potential, it should exhibit this potential not only during interaction with its own homolog, but also during interaction with nonhomologous and mixed acrocentrics. In that case the frequencies of associations of mixed and nonhomologous chromosomes ($i \neq j$) ought to be determined by the product of the associative potentials of the participating chromosomes ($a_i \cdot a_j$).

Accordingly, frequencies of associations of nonhomologous and mixed chromosomes were calculated from the value of associative potential thus obtained (Table 1). The theoretical frequencies which were found were about 4 times less than the empirical frequencies of the corresponding associations (Table 1). The discovery that the empirical frequencies were 4 times greater could be due to the twofold increase in associative potential of each acrocentric in the composition of associations of two nonhomologous and mixed chromosomes (Table 1).

Comparison by the χ^2 method revealed good agreement between the empirical and theoretical frequencies calculated with allowance for the twofold increase in associative potential of the chromosomes, so that the hypothesis of the twofold increase in associative potential of each acrocentric in the composition of associations of two nonhomologous and mixed chromosomes was not upset (Table 1).

The increase in associative potential could arise both as a result of an increase in the associative activity of the chromosomes themselves and, probably, also as a result of the presence of conditions in the cell favoring formation of associations of nonhomologous and mixed chromosomes. The term "associative potential" which we use takes into account not only the intrinsic activity of acrocentric chromosomes, but also the influence of extrachromosomal factors.

At the present time the property of acrocentric chromosomes of participating in associations is described by the terms: "associative tendency," "probability," and "activity." In my opinion the term "associative tendency" [4, 7] cannot be used in this case because the formation of associations is not a tendency, but a regular property of acrocentric chromosomes. The term "associative probability" [8, 10] is more theoretical in its meaning, for the word "probability" endows it with the sense of an expected, theoretically calculated probability of participation in association. The term "associative activity" ought to characterize only the intrinsic activity of acrocentric chromosomes. It does not take into account possible effects of extrachromosomal factors of the formation of associations. I prefer the term "associative potential" because it takes into account not only the intrinsic associative activity of the chromosomes, but also the influence of the cell. The concept of "associative potential" incorporates the notion of the ability of each acrocentric chromosome to participate in the formation of an association or to maintain associative connections under the influence of forces capable of breaking them.

The presence of two levels of associative potential of the chromosomes was thus discovered in two-chromosome associations. During interaction between two nonhomologous and mixed chromosomes their higher associative potentials are manifested, but these are reduced approximately by half during interaction between two homologous chromosomes. The character of the changes is more likely to be discrete, for the levels of associative potential possess quite definite values: for homologs $\bar{a}_i = 0.1462$ and $\sigma = 0.028$; for nonhomologous and mixed chromosomes $\bar{a}_i = K \cdot 0.1462$, where $K = 2.066$, and $\sigma = 0.1944$.

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