SYNAPTONEMAL COMPLEX CONFIGURATIONS IN ROBERTSONIAN HETEROZYGOTES

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We present here the classification of synaptonemal complex (SC) configurations in meiotic prophase I in animals heterozygous for Robertsonian (Rb) translocations on the basis of own studies and literature data. Configurations of SC multivalents, due to the homology of Rb metacentrics on one or both arms, as well as the ability of multivalents to form a temporary association, led to the formation of chromosome chains.

K e y   w o r d s: synaptonemal complex, Robertsonian translocation, heterozygote, multivalent, SC chain.

A b b r e v i a t i o n s: Rb — Robertsonian translocation, SC — synaptonemal complex.

Robertsonian (Rb) translocation, or centric fusion, a widespread type of chromosome rearrangements, is the joining of two acrocentrics at their centromere to form a metacentric. Rb fusion is a source of intraspecific chromosome variation. Animals with broad Rb polymorphisms are quite interesting, especially species those with an Rb fan (all acrocentrics of the initial karyotype may be included in the formation of Rb metacentrics): *Mus musculus*, *Sorex araneus*, *Ellobius tancrei* and others.

The synaptonemal complex (SC) is a multiproteinaceous tripartite structure that forms between homologous chromosomes in prophase I of meiosis. The SC analysis allows us to trace all details of the formation of its axial elements, from the beginning of pairing and synapsis at the zygotene, in particular synapsis and its correction in heterozygotes for chromosome rearrangements at the pachytene and desynapsis dynamics at diplotene.

In Rb heterozygotes, various types of SC multivalents are formed at prophase I (Bogdanov et al., 1986; Johannisson, Winking, 1994). SC configuration can influence changes in the architecture of meiotic nuclei and thus lead to the formation of unbalanced gametes and reduce fertility overall (King, 1993). The present report is devoted to the analysis of SC's structure and behavior in Rb heterozygotes of several mammalian species and interspecific hybrids, including *Ellobius tancrei*, *S. araneus*, *Cricetulus barabensis*, *Allocricetulus eversmanni* and *A. curtatus*. We offer a classification of SC configurations in heterozygotes for Rb fusions based on our own studies and literature data.

Materials and Methods

We investigated mammals heterozygous for Rb translocations: F$_1$ hamster hybrids (2n = 23) between *C. barabensis pseudogriseus* (2n = 24) and *C. barabensis griseus* (2n = 22) (obtained from A. V. Surov and V. M. Malygin); F$_1$ hamster hybrids (2n = 23) between *A. curtatus* (2n = 20) and *A. eversmanni* (2n = 26) (from A.V. Surov and N. Yu. Feoktistova); F$_1$ mole vole hybrids (2n = 50) between *E. tancrei* (2n = 50) and *E. tancrei* (2n = 50) from different localities (hybrids were obtained by the courtesy of I. Yu. Bakloushinskaya and E. A. Lyapunova); common shrew hybrids (2n = 21) from the Moscow-Neroosa contact zone (from S. V. Pavlova).

SC preparations were prepared and fixed using the corresponding technique (Navarro et al., 1981) with some modifications. Slides were stained with a 50 % AgNO$_3$ solution in a humid chamber for 3 h at 56 °C, washed 4 times in distilled water and air dried. Stained slides were examined in a JEM 100B electron microscope.

Results

Animals heterozygous for a single Rb translocation have one SC trivalent in pachytene meiocytes. Complete synapsis between the Rb metacentric and two acrocentrics of SC trivalents was identified in an early pachytene nuclei in the F1 *Cricetulus* hybrid (Fig. 1, *a*). We call these SC trivalents «quick» (Fig. 3, *a*), following the earlier terminology (Kolomiets et al., 1985). Heterozygous *Ellobius tancrei* have both «quick» and «slow» SC trivalents (no complete synapsis in mid-late pachytene) (Fig. 1, *b*; 2; 3, *b*).

A special type of temporary SC configurations are chains which are formed several open SC trivalents. This association of chromosome trivalents in the chain is due to synapsis between the acrocentric short arms of different SC trivalents (Fig. 1, *b*; 3, *c*). Previously, these chains of SC trivalents were described in *E. tancrei* males heterozygous for 10 Rb metacentrics (Kolomiets et al., 1985; Bogdanov et al., 1986).

If the karyotypes of individuals from different populations have two monobrachial homologous metacentrics, the heterozygous spermatocytes and oocytes have open SC tetravalents consisting of two metacentrics and two acrocentrics.
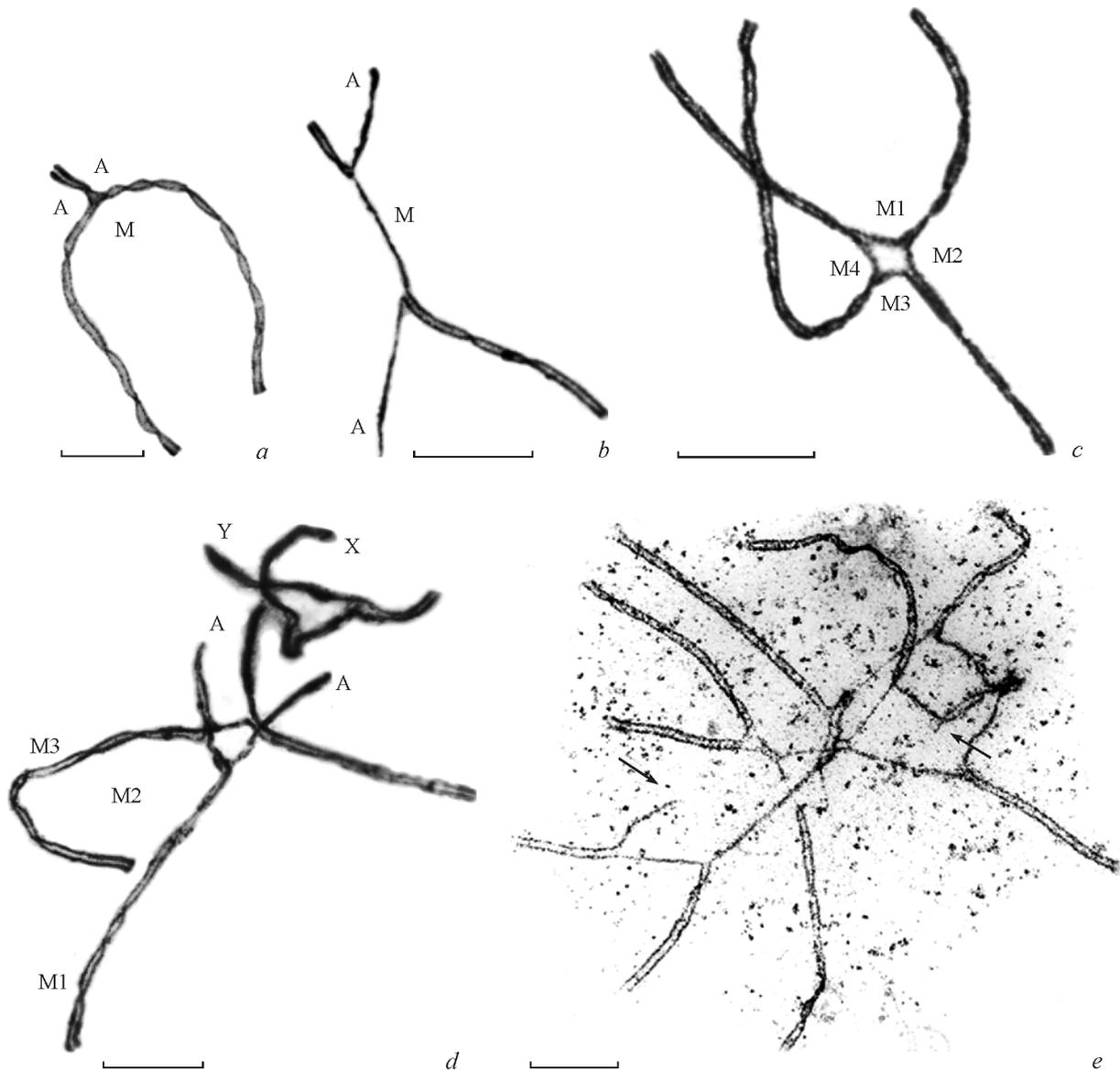
Fig. 1. Electron micrographs of synaptonemal complex (SC) configurations from the Robertsonian translocation (Rb) heterozygotes.
a — *Cricetulus barabensis* closed trivalent; *b* — *Ellobius tancrei* open trivalent; *c* — *Sorex araneus* closed tetravalent; *d* — *Allocricetulus (eversmanni × curtatus)* open pentavalent with XY bivalent; *e* — *Ellobius tancrei* complex SC chain (for more details see Matveevsky et al., 2015a). Ends are marked with *arrows*. A — acrocentric, M — metacentric *Scale bar* = 2 μm.

We have identified an open SC pentavalent, which is formed by three metacentrics with monobrachial homology (i. e., two metacentrics shared homology in the single arm) and two acrocentrics (class II, with monobrachial homologous Rb meta-/submetacentrics) in *Allocricetulus* hybrids (Fig. 1, *d*; 3, *e*). We detected closed SC trivalents (class I, without monobrachial homologous Rb meta-/submetacentrics) and one open SC tetravalent formed by two metacentrics with monobrachial homology and two acrocentrics (class II) in *E. tancrei* heterozygotes for three Rb metacentrics.

SC tetravalents formed in the meiotic nuclei of heterozygotes for the four monobrachial homologous Rb metacentrics (class II). For example, we show a closed SC tetravalent from a spermatocyte of the common shrew from the hybrid zone between the Moscow and Neroosa races, differing in four metacentrics with monobrachial homology (Fig. 1, *c*; 3, *d*) (Matveevsky et al., 2012).

It should be noted that the formation of open chromosome chains may be the cause of the association of partially unsynapsed acrocentric sites with sex bivalent (Fig. 3, *h*). This can lead to impaired formation of a sex body (sign of spermatogenesis arrest). Data on reduced fertility in males heterozygous for multiple Rb translocations have been described by many authors (King, 1993).

Discussion

Since Rb translocations are widespread among animals, the formation of SC configurations is similar in simple and complex heterozygotes of different taxonomic groups (Table).

In hybrids between *E. tancrei* chromosomal forms, the different types of SC configurations have been described. In
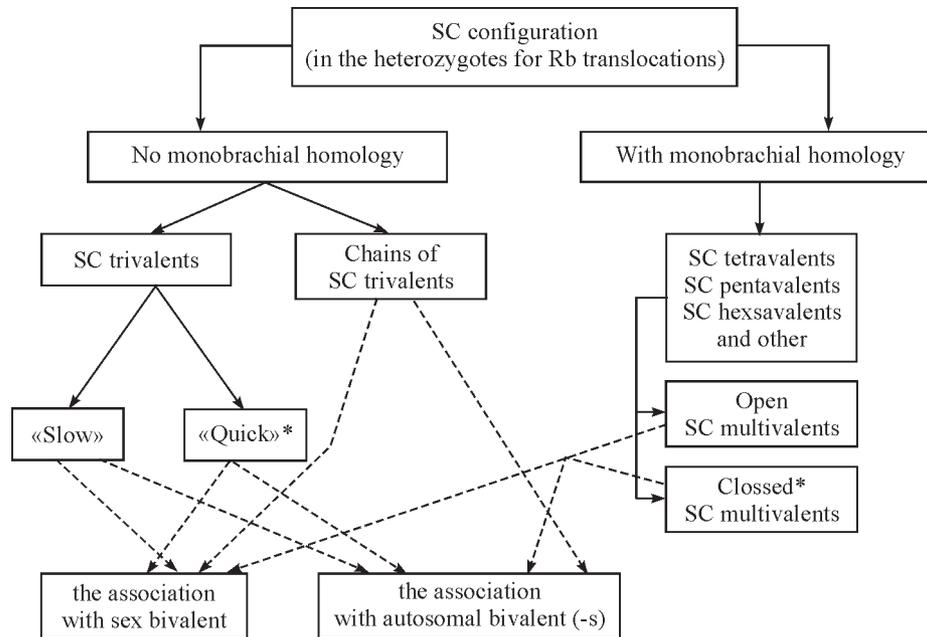
Fig. 2. Synaptonemal complex (SC) configurations classification in the Robertsonian translocation (Rb) heterozygotes.
* Associations are possible in the case of forming a triple SC.

the nuclei of F1 spermatocytes (2n = 44), hybrids from crossing 2n = 54 and 2n = 34 were expected to have six SC bivalents, a sex bivalent, and 10 SC trivalents, each was formed as a result of the synapsis of one Rb metacentric and two acrocentrics. However, the expected pattern could be observed only in a single nucleus at late pachytene. It was found that chromosome synapsis in forming trivalents in most cases was slower than bivalent synapsis (Kolomiets et al., 1986). The process of the formation of axial elements slows down in the central part of Rb metacentrics from SC trivalents, which were highly extended between the points of attachment to the nuclear envelope. There were gaps in the pericentromeric area of the metacentric axis until the mid pachytene.

Such «delayed» or «slow» SC trivalents (Fig. 3, *b*) can form a free closed SC trivalent at the mid pachytene. However, some trivalents are combined into a chain, which we provisionally named class I chains (Fig. 2). This is the temporary configuration in which the open («yet to be formed») SC trivalents are connected to each other via the SC between short arms of acrocentrics from neighboring SC trivalents. Such chains fall to the end of prophase I (as a rule, in only single nuclei) (Kolomiets et al., 1985; Bogdanov et al., 1986). The fertility of such hybrids was reduced, the causes of which may have been damage during the formation of the chiasma; errors during chromosome segregation at anaphase I and, as a consequence, the arrest in metaphase and anaphase I; gamete aneuploidy may have also occurred in offspring. It is not possible to completely exclude a mechanism of pachytene arrest, as disturbances were observed in single nuclei in the structure and behavior of the sexual bivalent. It did not form a sex body, and remained in the center of the nucleus, open at one end of the bivalent.

Class II chains were formed due to monobrachial homology. If the chain contained only monobrachially homologous Rb metacentrics, the closed chain formed. If the hybrids had an Rb metacentric, one arm of which was homologous to the acrocentric, and the other homologous to the arm of another Rb metacentric, an open chain formed. However, such chains

can form a temporarily closed configuration; in this case, the chain is closed by short SC fragments between the short arms of non-homologous acrocentrics, similar to class I chains. A closed class II chain (pentavalent, formed by the three Rb submetacentrics and two acrocentrics) was found in the nuclei of F1 hybrids (2n = 49) of *E. tancrei* (Bakloushinskaya et al., 2010). However, in other F1 hybrids (2n = 50), a complex SC chain (Fig. 1, *e*) was revealed in pachytene oocytes.

SC chains and rings, which include Rb metacentrics, were described in other species as well. For example, the class II chain was described in the interracial hybrid of the common shrew, *Sorex araneus*, caught in the hybrid zone of Moscow (2na = 18) and Seliger (2na = 20). In spermatocytes of this hybrid, a theoretically expected chain was revealed, which was an open multivalent formed by 11 axial elements, 9 Rb metacentrics and two acrocentrics (Pavlova et al., 2008). A study of the SC in hybrids of *M. domesticus*, obtained by crossing forms from Campobasso (2n = 22, NF = 40) and Cittaducale (2n = 22, NF = 40) is of the particular interest (Johannisson, Winking, 1994). In these hybrids a closed ring multivalent formed that included 16 Rb metacentrics. Examples of different SC configurations are shown in Table.

The analysis of the SC configuration in Rb heterozygotes has to be based on karyotype data from each hybrid. There may be some difficulties in identifying SC trivalents in the early stages of meiotic prophase I because of incomplete chromosome synapsis and a delay of the metacentric axial element formation of centromeric regions in «slow» SC trivalents. Slow SC trivalents at early pachytene look like two SC bivalents (they are pseudobivalents). Therefore, electron microscopic analysis of SC needs to be carried out in the later stages of prophase I. Immunocytochemical studies using antibodies to kinetochore proteins (centromere) would be an important addition to electron microscopy data.
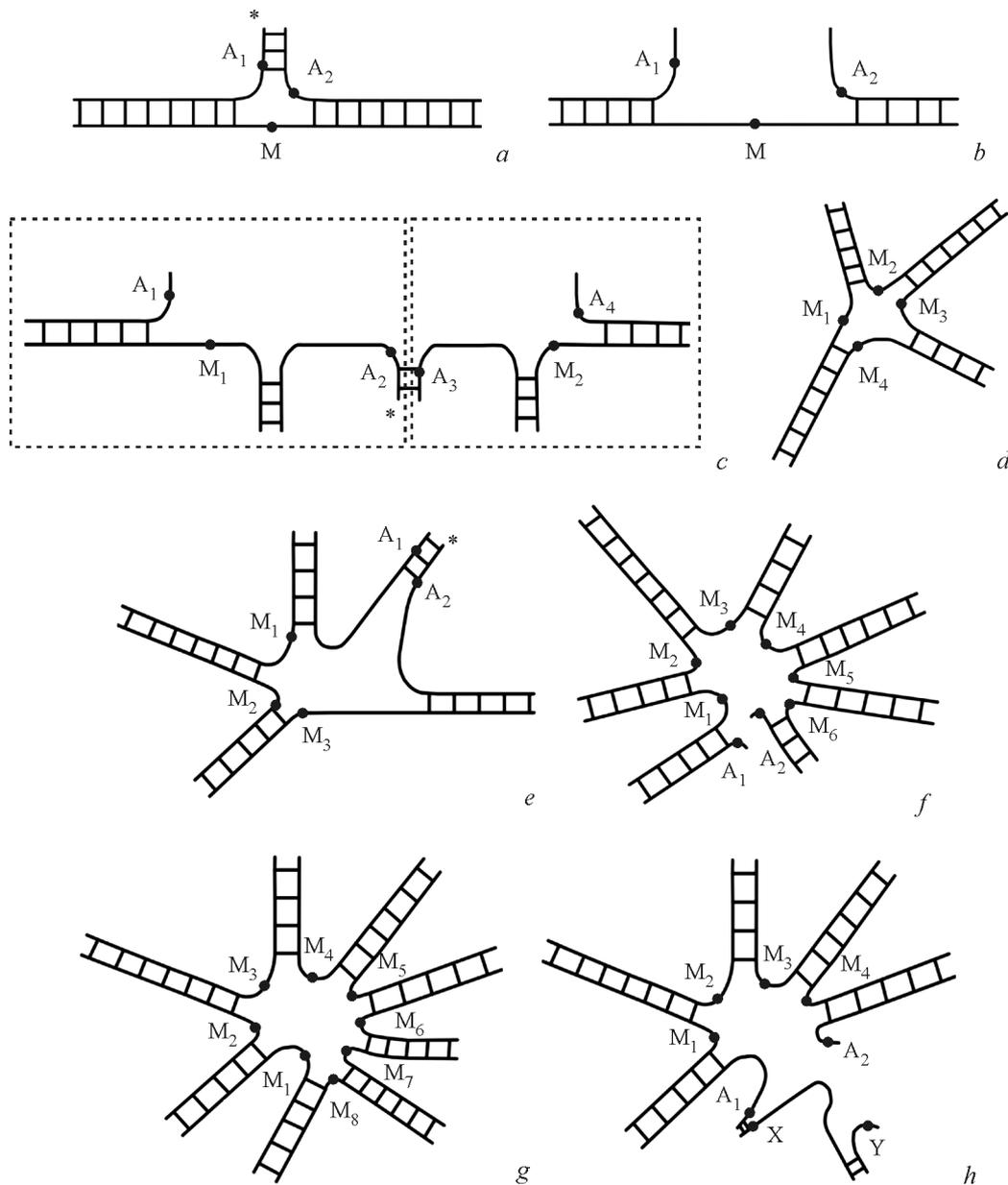
Fig. 3. Schemes of synaptonemal complex (SC) configurations in the Robertsonian translocation (Rb) heterozygotes.

a — quick SC trivalent; *b* — slow SC trivalent; *c* — SC trivalents chain; *d* — closed SC tetravalent; *e* — closed SC pentavalent; *f* — open SC multivalent; *g* — closed SC multivalent; *h* — SC multivalent — sex bivalent association. A — acrocentric, M — metacentric, * — nonhomologous synapsis.

Characteristics and examples of some SC configurations in the Rb heterozygotes

SC configuration	Explanations	Examples
«Quick» SC trivalents	Trivalents form SCs between short arms of acrocentics at the late zygotene — early pachytene	*E. tancrei* (Kolomiets et al., 1986); *Eulemur* (Ratomponirina et al., 1988); *Nannospalax ehrenbergi* Nehring 1898 (Wahrman et al., 1985; Matveevsky et al., 2015b); *Akodon molinae* Contreras, 1968 (Fernández-Donoso et al., 2001); *Mus musculus* Linnaeus, 1758 (Manterola et al., 2009), *Cricetulus barabensis* Pallas, 1773 (Matveevsky et al., 2014)
«Slow» SC trivalents	Trivalents have asynapsed SC's zone. The synapsis, as a rule, ends at late pachytene	*E. tancrei* (Kolomiets et al., 1986); *Eulemur* (Ratomponirina et al., 1988); *M. musculus* (Manterola et al., 2009); *Ctenomys perrensi* Thomas, 1898 (Lanzone et al., 2007)
Chains of SC trivalents	Shorts arms of acrocentrics, joined to two or more «slow» trivalents, have heterosynapsed SC's parts	*E. tancrei* (Kolomiets et al., 1985; Bogdanov et al., 1986)

Characteristics and examples of some SC configurations in the Rb heterozygotes

SC configuration	Explanations	Examples
Closed SC tetravalents	SC tetravalents are closed due to homologous sypapsis or heterosynapsis of the short arms of acrocentrics	*E. tancrei* (Lyapunova et al., 1980); *Bothriurus araguayae* Vellard, 1934 (Schneider et al., 2009); *S. araneus* (Narain, Fredga, 1997, 1998; Matveevsky et al., 2012)
Open SC multivalents	Some axial elements of SC multivalents do not undergo synapsis	*M. musculus* (Johannisson, Winking, 1994); *S. araneus* (Karamysheva et al., 2007; Pavlova et al., 2008); *Eulemur* (Ratomponirina et al., 1988); *Allocricetulus* Argyropulo, 1933 (Gureeva et al., 2015 and this article); *E. tancrei* (Matveevsky et al., 2015a and this article)
Closed SC multivalents	SC multivalents closed due to synapsis of homologous arms or heterosynasis of short arms of acrocentrics	*M. musculus* (Johannisson, Winking, 1994); *E. tancrei* (Bakloushinskaya et al., 2010; Matveevsky et al., 2015a)
SC trivalents chains or open SC multivalents with sex bivalent association	SC trivalents inside chains and open SC trivalents have long axial elements, which synapsed with axial elements of sex bivalent	*M. musculus* (Johannisson, Winking, 1994); *Eulemur* (Ratomponirina et al., 1988; Djlelati, 1997); *E. tancrei* (Matveevsky et al., 2015a)

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КОНФИГУРАЦИИ СИНАПТОНЕМНЫХ КОМПЛЕКСОВ У РОБЕРТСОНОВСКИХ ГЕТЕРОЗИГОТ

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На основе собственных исследований и данных литературы приведены сведения о конфигурациях синаптонемных комплексов (СК) в профазе I мейоза у животных, гетерозиготных по Робертсоновским (Rb) транслокациям. Конфигурации СК-мультивалентов обусловлены гомологией Rb-метацентриков по одному или обоим плечам, а также способностью мультивалентов к временной ассоциации, приводящей к формированию цепочек хромосом.

К л ю ч е в ы е с л о в а: синаптонемный комплекс, Робертсоновская транслокация, гетерозигота, мультивалент, цепочка СК.

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