

Z. Säugetierkunde 53 (1988) 148–161
© 1988 Verlag Paul Parey, Hamburg und Berlin
ISSN 0044-3468

Robertsonian karyotype variation in the European house mouse, *Mus musculus*

Survey of present knowledge and new observations

By H. WINKING, BEATRICA DULIĆ, and G. BULFIELD

Institut für Biologie der Medizinischen Universität zu Lübeck, Institute of Zoology, University of Zagreb, and Institute of Animal Physiology and Genetics Research, Roslin, Midlothian

Receipt of Ms. 26. 1. 1987

Abstract

The karyotype of the European long-tailed house mouse, *Mus musculus*, was studied from Zadar (Yugoslavia) and Ammoudia (Greece). In mice from Zadar six and in those from Ammoudia three Robertsonian (Rb) chromosomes were present and have been identified by their G-band pattern. The composition of some of these marker chromosomes was unknown before, whereas some have been found to occur in other, geographically separated populations. The karyological details of both populations of the East-European distribution area were discussed together with observations on the karyotype of mice from Central and Western Europe and from Northern Africa.

Fertility data of a feral mouse from Zadar, which was heterozygous for one Rb chromosome, show that this particular genotype does not necessarily imply impairment of fertility in wild mice, which is mainly present in Rb heterozygous animals with a mixed genetic background of wild and laboratory mice. The Rb heterozygosity dependent impairment of fertility is due to segregational disorders during meiosis I.

Introduction

EVANS et al. (1967) and LEONARD and DECKNUDT (1967) were first to report the occurrence of a metacentric chromosome in laboratory mouse strains, and more findings of the same kind became known thereafter (see GROPP and WINKING 1981). Similar changes, though with multiple pairs of metacentric chromosomes, were detected shortly later in wild mice from the Poschiavo valley in Southern Switzerland (GROPP et al. 1970), as well as from other areas of the Rhaetian Alps (GROPP et al. 1972). It became clear that these observations correspond to chromosome rearrangements in a complex system of balanced Robertsonian (Rb) variation, i.e. to changes due to centric translocations of two acrocentric chromosomes and commensurate reduction of the total number of chromosomes (MATTHEY 1966). The before mentioned and subsequent reports (CAPANNA et al. 1976; v. LEHMANN and RADBRUCH 1977; DULIĆ et al. 1980; ADOLPH and KLEIN 1981, 1983; GROPP et al. 1982; SAID et al. 1986) dealt with the occurrence, composition and characteristics of Rb metacentric chromosomes in mice obtained from local populations in the central (Lombardy, Switzerland, Germany), southern (Appennines, Sicily), or western (Spain, Scotland) Europe and North Africa (Tunisia). Only little information exists, however, about the karyotype patterns of house mouse populations from eastern and southeastern Europe. It appeared worthwhile to supplement the so far scarce cytogenetic data about this region by new and recent observations on mice from Yugoslavia and Greece, and to collect available, though scattered, karyogeographic data for an update comprehensive survey of the occurrence and distribution of Rb chromosome variability in the house mouse, including the derived laboratory strains.

Material and methods

Sixteen mice were trapped on two occasions near Zadar (Dalmatia), namely 10 animals in 1978 and six animals in 1981. A second site of investigation, about 640 kms southeast on the Adriatic-Ionian coast-line, is Ammoudia (Epiros: Northeastern Greece) from where 19 mice were analysed in 1980.

Karyotypes were established on lymphocyte metaphases from short time cultures (TRIMAN *et al.* 1975) of peripheral blood cells. The blood samples were obtained by puncture of the retro-orbital sinus taken either from the original wild trapped mice (Zadar) or from their F-1 offspring with DBA/2 females (Greece). The identification of individual chromosomes was made on G-banded metaphases (SEABRIGHT 1971) using the criteria of the standard mouse karyotype presented by NESBITT and FRANKE (1973). The designation of the Rb metacentric chromosomes and the arm composition followed the rules of the Committee on Standardized Nomenclature for Mice (1979). In addition, fertility of one natural male hybrid (Zadar) and of laboratory bred males derived from an interpopulation cross (Zadar \times Poschiavo, see Table 4) was assessed by evaluation of matings with normal fertile laboratory female mice and by testis histology.

Results

Chromosome findings in mice from Zadar (Dalmatia)

The cytogenetic findings, in particular the observation of Rb metacentric chromosomes and their arm composition, are recorded in Table 1. 15 among the 16 animals showed a homozygous karyotype with six pairs of metacentric chromosomes and seven pairs of acrocentric autosomes plus the sex chromosome pair (Fig. 1). The remaining individual, which belonged to the 1978 sample, exhibited homozygosity for five pairs of Rb metacentrics only, and heterozygosity for the Rb(8.17)38Lub metacentric, corresponding to a karyotype with an odd number of 11 metacentrics, 16 acrocentrics and the sex chromosomes.

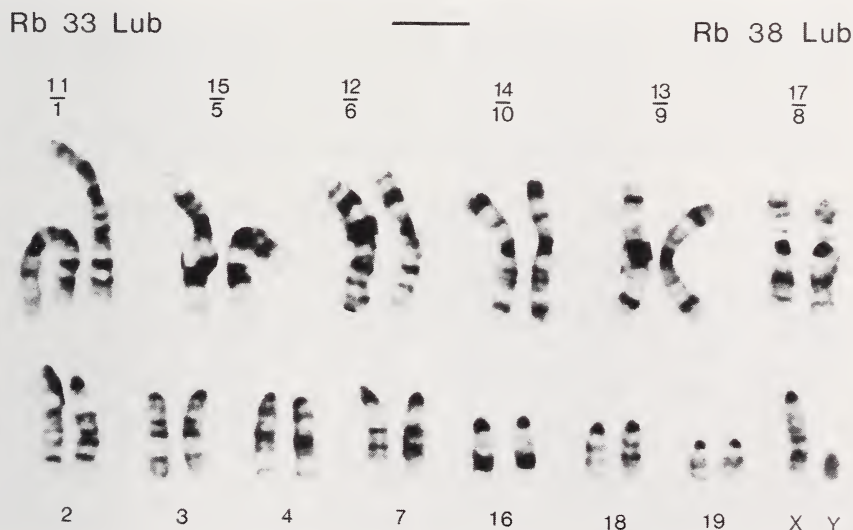


Fig. 1. G-banded karyotype of a male mouse from Zadar (Yugoslavia) with six pairs of Rb chromosomes. Numbers refer to chromosomes of the standard karyotype of the mouse

Chromosome findings in mice from Ammoudia (Greece)

The karyotype of 19 wild trapped males was established by studying their 34 offspring from crosses with DBA/2 females. In conventional chromosome preparations obtained from the F-1 progeny of 19 feral males, none, one or two Rb translocation metacentrics were found. However, from G-banding analyses it could be inferred that three different Rb translocations with a 3.10, 5.12 and 15.17 composition are present in this population (Table 2). The cytogenetic findings in the analysed progeny of the 19 wild trapped males are summarized in Table 2. From the mode of transmission of the Rb metacentric chromosome into the F-1 descendants, it can be concluded that eight of the original males must have been heterozygous for one or more Rb translocations. Interestingly heterozygosity for all three Rb chromosomes of the investigated population must have occurred in at least one of the original males. This indicates that the Ammoudia mouse population is very heterogeneous. It seems possible that a few more Rb metacentric chromosomes are present in the small sample investigated, but were not transmitted to the limited number of karyotyped F-1 offspring.

Table 1. Arm composition and designation of Rb translocations of mice trapped near Zadar (Yugoslavia) and Ammoudia (Greece)

Rb translocations found in mice from	
Zadar ¹	Ammoudia ²
Rb (1.11) 33 Lub	Rb (15.17) 64 Lub
Rb (5.15) 34 Lub	Rb (3.10) 65 Lub
Rb (6.12) 35 Lub	Rb (5.12) 66 Lub
Rb (10.14) 36 Lub	
Rb (9.13) 37 Lub	
Rb (8.17) 38 Lub	

¹ Populations highly homogeneous for Rb translocations: 15 among 16 animals were homozygous for all of the six Rb chromosomes (see text). – ² Population highly heterogeneous for Rb translocations (see Table 2 and text)

Table 2. Karyotype of first or second offspring of wild males (Ammoudia) with DBA/2 females

Current no of wild males	first	Karyotypes of or	second progeny
1	acrocentrics only		Rb (3.10) 65 Lub/+
2	acrocentrics only		Rb (3.10) 65 Lub/+
3	Rb (3.10) 65 Lub/+		Rb (3.10) 65 Lub/+
4	Rb (3.10) 65 Lub/+		Rb (3.10) 65 Lub/+
5	acrocentrics only		acrocentrics only
6	acrocentrics only		Rb (15.17) 64 Lub/+
7	acrocentrics only		Rb (15.17) 64 Lub/+
8	acrocentrics only		–
9	Rb (3.10) 65 Lub/+		Rb (3.10) 65 Lub/+ and Rb (5.12) 66 Lub
10	acrocentrics only		–
11	Rb (5.12) 66 Lub/+ and (Rb (15.17) 64 Lub		Rb (15.17) 64 Lub/+
12	Rb (3.10) 65 Lub/+		Rb (3.10) 65 Lub/+
13	acrocentrics only		Rb (15.17) 64 Lub/+
14	Rb (3.10) 65 Lub/+		Rb (3.10) 65 Lub/+
15	acrocentrics only		acrocentrics only
16	acrocentrics only		Rb (3.10) 65 Lub/+
17	acrocentrics only		acrocentrics only
18	Rb (3.10) 65 Lub/+		–
19	Rb (3.10) 65 Lub/+		–

Karyogeographic evaluation of the findings in Zadar and Ammoudia

Three of the Rb metacentric chromosomes found in Zadar (Dalmatia), i.e. (6.12), (10.14) and (8.17), show an arm composition identical to Rb chromosomes found in a mouse

population near Palermo (v. LEHMANN and RADBRUCH 1977), and two of them, (10.14) and (8.17), were shown to occur in mice from southern Germany (ADOLPH and KLEIN 1981). The Rb metacentric chromosome with the (5.15) arm composition occurs in a wide geographical range between Zadar (Dalmatia), central and northern Italy, Switzerland (CAPANNA et al. 1976; GROPP et al. 1982) and Spain (ADOLPH and KLEIN 1981). Hence, the geographical distribution of this particular Rb metacentric chromosome follows an eastward direction. The (1.11) chromosome is likewise present in the northern African population (Monastir, Tunisia: SAID et al. 1986), but the (9.13) chromosome of the Zadar population as well as two of the three Rb chromosomes of the Ammoudia (Greece) mice, i.e. (3.10) and (5.12) are unique among the Robertsonian chromosomes so far known from feral mouse populations (GROPP and WINKING 1981; BROOKER 1982; ADOLPH and KLEIN 1981; 1983).

Fertility of the natural hybrid found in Zadar

Heterozygosity of metacentrics of feral origin within a laboratory mouse genome may cause meiotic anaphase I nondisjunction. This leads to the formation of unbalanced gametes which transmit the aneuploid genome into the zygote. As a consequence the litter size is reduced at a commensurate rate, since whole arm aneuploidies are subject to selective elimination during pregnancy (CATTANACH and MOSELEY 1973; GROPP et al. 1974). While such segregational disorders are mainly known from heterozygotes for Rb translocations introduced from feral mice into laboratory strains, no comparable knowledge exists about Rb heterozygosity in a natural population. Therefore, the Zadar male with Rb(8.17)38Lub heterozygosity was mated several times with all acrocentric outbred NMRI females. The pregnant mothers were sacrificed at day 13 of pregnancy (plug day = day 1) and the numbers of corpora lutea and implants were recorded. Chromosome preparations were made from the fetal membranes of all alive implants. For comparison breeding records were established from males with the same Rb chromosome after introduction by five consecutive backcrosses into a laboratory mouse genome (NMRI) and from other Rb(8.17) heterozygous males, whose 8.17 Rb chromosome had a different source. One of these is the Rb(8.17)1Iem chromosome detected by BARANOV and DYBAN (1971) in a laboratory strain, and a second one is the Rb(8.17)6Sic chromosome isolated from a wild mouse of a Sicilian population with a series of seven metacentrics (v. LEHMANN and RADBRUCH 1977). This latter chromosome has been isolated and is now carried on a mixed background of wild and laboratory derived genes. The results of the breeding experiments as shown in Table 3 provide no evidence for the existence of noteworthy

Table 3. Effect of heterozygosity in males for Rb (8.17) translocations of different origin upon fertility¹

Rb chromosome	pregnant ♀♀	no of corpora lutea	implants	resorptions	percentage of euploid implants	aneuploid implants
Rb (8.17) 38 Lub/+ natural hybrid	7	86	80	1.3	98.7	—
Rb (8.17) 38 Lub/+ laboratory mouse genome	14	177	152	38.8	61.2	—
Rb (8.17) 6 Sic/+ laboratory mouse genome	10	139	121	19.8	79.3	0.9 ²
Rb (8.17) 1 Iem/+ laboratory mouse genome	10	144	126	9.5	90.5	—

¹ Data refer to observations on fetal progeny at day 13 sired by heterozygous fathers and all acrocentric mothers (NMRI). — ² One embryo with 39 chromosome arms; presumably XO

disturbances of meiotic segregation in the Rb(8.17)38Lub/+ natural hybrid male, since the day 13 fetal progeny contains only a very low rate of resorptions. In addition there is no evidence for an increased rate of preimplantation losses. While the respective proportions of preimplantation losses are in the same low range in the progeny of both other Rb(8.17) heterozygotes, these show higher postimplantation losses than the Rb38Lub heterozygous feral male. Surprisingly the highest postimplantation losses, however, were found in crosses with Rb(8.17)38Lub/+ males, which carried the Rb chromosome in a laboratory mouse genome. The correspondence of the respective proportions of aneuploid MII plates in Rb11em/+, Rb6Sic/+ and Rb38Lub/+ males with a laboratory mouse genome to the resorption rates lead us to assume that a major part of the resorptions is caused by chromosomal imbalance of the fetuses. In the Rb38Lub/+ feral male, even though MII evaluations were not possible, since the only available male died prior to the end of the breeding experiments, a correspondence of meiotic malsegregation rates and postimplantation losses has to be postulated.

Cytogenetic and reproductive analysis of laboratory hybrids bred from "Zadar" with multimetacentric type mice of different origin

Breeding assays of animals with newly identified Rb translocations against mice with a set of already known Rb chromosomes bear two advantages. Firstly, the type of pairing figures observed in 1st meiotic prophase can be used for examination on the correctness of the arm assignments of Rb translocations. Secondly, it provides information about the influence of complex Rb heterozygosity upon fertility. Both aims were borne in mind when males of the Zadar colony were crossed with females with the Rb1Bnr-7Bnr chromosome set ("tobacco mouse" – poschiavinus type). In case of proper identification of the "Zadar" metacentric chromosomes (see Tab. 1), the six "Zadar" and the seven "poschiavinus" metacentrics should be arranged in meiotic prophase of the hybrids in two chains of six and of five Rb metacentrics plus one ring bivalent of metacentric chromosomes. In fact, such pattern was observed in diakinesis figures. The male hybrids with such chains were sterile, and in the testis a severe manifestation of spermatogenetic arrest was observed in histological sections suggesting a breakdown of spermiogenesis during meiosis or shortly thereafter. This finding supports observations reported by SEARLE et al. (1978), EVANS (1976) and GROPP et al. (1982) that chain formation during prophase of meiosis I has a harmful effect upon the process of spermatogenesis.

Discussion

Survey of a present knowledge about Robertsonian variation in laboratory and wild caught mice

By means of biochemical and morphological characteristics two groups within the species *Mus musculus* can be recognized in Europe (ZIMMERMANN 1949; THALER et al. 1981).

Geographically one group consisting of the three subspecies "*domesticus*", "*brevirostris*" and "*praetextus*" occupies areas west of a line running from the Baltic sea through Germany and down to the Black sea. The second group taxonomically designed as *M. m. musculus* is distributed east to the beforementioned borderline (see: ORSINI et al. 1983 and Fig. 2). Besides *M. musculus*, at least, two further *Mus* species exist in Europe occurring sympatrically with one or the other of the *M. musculus* subspecies, namely *M. spretus* in southwestern Europe and one *Mus* species in southeastern Europe, which is known as *Mus 4* (THALER et al. 1981). A common karyological denominator to all these species are acrocentric chromosomes, and an all acrocentric karyotype can be considered as the



Fig. 2. Geographical sites of house mouse populations with Rb chromosomes in Western Europe and Northern Africa. Characteristics of each population are given in Tab. 4. Solid line represents borderline of the western and eastern subspecies of *M. musculus* (see: ORSINI et al. 1983)

standard karyotype of the longtailed house mouse, *M. musculus*, as well as of the Asiatic subspecies of the house mouse.

The presence of Robertsonian translocations is a special trait of the *domesticus*, *brevirostris*, *praetextus* group of *M. musculus*. Moreover, this karyotypic variability seems to be limited to the European and African distribution area of house mice of this group. Altogether 22 different and characteristic Rb-constitutions have been found in the western part of Europe and Africa. The locations and the combinations of Rb-chromosomes present are listed in Fig. 2 and Table 4. Although "*domesticus/brevirostris*" type mice invaded large areas outside Europe along the routes of world traffic, at least few reports exist on the presence of Robertsonian translocations in natural populations like in Marion Island (ROBINSON 1978) far outside of Europe. In addition, two further reports about the occurrence of Robertsonian translocations in Asiatic house mice exist in the literature (CHAKRABARTI and CHAKRABARTI 1977; MORIWAKI et al. 1984). On the other hand, spontaneous Rb variation is known to occur in laboratory mice, whose biochemical and mitochondrial DNA characteristics have been shown to belong mainly to a "*domesticus*" background (YONEKAWA et al. 1980; FERRIS et al. 1982). Altogether 22 different Rb metacentrics have been described in laboratory stocks (see: GROPP and WINKING 1981; SEARLE and BEECHEY 1986). In contrast to wild mice all autosomes are involved in laboratory-type Rb translocations. In addition, one case of an X-chromosome translocation onto autosome 3 (ARROYO NOMBELA and RODRIGUEZ MURCIA 1977) has been described. In contrast, a Robertsonian Y-autosome translocation has never been observed.

Table 4. Arm composition, designation and derivation of Rb-chromosomes in feral mouse populations of Europe and northern Africa

Arm composition/ designation	Locality	No of locality (see Fig. 2)	References	Arm composition/ designation	Locality	No of locality (see Fig. 2)	References
Rb (1.11) 33 Lub Rb (5.15) 34 Lub Rb (6.12) 35 Lub Rb (10.14) 36 Lub Rb (9.13) 37 Lub Rb (8.17) 38 Lub	Zadar	1	this paper	Rb (2.4) 25 Lub Rb (3.6) 26 Lub Rb (5.15) 27 Lub Rb (7.8) 28 Lub Rb (10.12) 29 Lub Rb (11.13) 30 Lub Rb (9.14) 31 Lub Rb (16.17) 32 Lub	several places near Milano	8	GROPP et al. 1982
Rb (15.17) 64 Lub Rb (3.10) 65 Lub Rb (5.12) 66 Lub	Am- moudia	2	this paper	Rb (3.4) 39 Lub Rb (2.8) 40 Lub Rb (6.7) 41 Lub Rb (5.15) 42 Lub Rb (10.12) 43 Lub Rb (11.13) 44 Lub Rb (9.14) 45 Lub Rb (16.17) 46 Lub	Gallarate	9	WINKING and GROPP 1983
Rb (3.4) 1 Sic Rb (2.15) 2 Sic Rb (6.12) 3 Sic Rb (5.13) 4 Sic Rb (10.14) 5 Sic Rb (8.17) 6 Sic Rb (9.16) 7 Sic	Palermo	3	V. LEH- MANN and RAD- BRUCH 1977	Rb (1.6) 47 Lub Rb (3.4) 48 Lub Rb (2.8) 49 Lub Rb (5.15) 50 Lub Rb (10.12) 51 Lub Rb (11.13) 52 Lub Rb (9.14) 53 Lub Rb (16.17) 54 Lub Rb (7.18) 55 Lub	Cremona	10	GROPP and WINKING 1981
Rb (1.2) 18 Lub Rb (4.13) 19 Lub Rb (3.9) 20 Lub Rb (5.14) 21 Lub Rb (8.12) 22 Lub Rb (10.15) 23 Lub Rb (6.16) 24 Lub	Island of Lipari	4	GROPP and WINKING 1981	Rb (1.3) 1 Lub Rb (2.8) 2 Lub Rb (4.6) 3 Lub Rb (5.15) 4 Lub Rb (10.12) 5 Lub Rb (11.13) 6 Lub Rb (9.14) 7 Lub Rb (16.17) 8 Lub Rb (7.18) 9 Lub	Bergamo, Ardenno, Sondrio	11	GROPP et al. 1982
Rb (1.18) 10 Rma Rb (2.17) 11 Rma Rb (4.11) 12 Rma Rb (6.7) 13 Rma Rb (3.13) 14 Rma Rb (5.15) 15 Rma Rb (8.14) 16 Rma Rb (10.12) 17 Rma Rb (9.16) 18 Rma	Campo- basso	5	CAPANNA et al. 1976	Rb (1.3) 56 Lub Rb (2.8) 57 Lub Rb (4.6) 58 Lub Rb (5.15) 59 Lub Rb (10.12) 60 Lub Rb (11.13) 61 Lub Rb (9.14) 62 Lub Rb (16.17) 63 Lub	Sondalo	12	GROPP et al. 1982
Rb (1.7) 1 Rma Rb (3.8) 2 Rma Rb (6.13) 3 Rma Rb (4.15) 4 Rma Rb (10.11) 5 Rma Rb (2.18) 6 Rma Rb (5.17) 7 Rma Rb (12.14) 8 Rma Rb (9.16) 9 Rma	Cittaduc- cale	6	CAPANNA et al. 1976	Rb (1.3) 1 Bnr Rb (4.6) 2 Bnr Rb (5.15) 3 Bnr Rb (11.13) 4 Bnr Rb (8.12) 5 Bnr Rb (9.14) 6 Bnr Rb (16.17) 7 Bnr	Brusio, Sondalo	13	GROPP et al. 1970; 1982
Rb (1.2) 10 Lub Rb (5.13) 11 Lub Rb (3.9) 12 Lub Rb (4.17) 13 Lub Rb (6.16) 14 Lub Rb (8.14) 15 Lub Rb (10.12) 16 Lub Rb (11.15) 17 Lub	Ancarano	7	GROPP and WINKING 1981				

Table 4 (continued)

Arm composition/ designation	Locality	No of locality (see Fig. 2)	References	Arm composition/ designation	Locality	No of locality (see Fig. 2)	References
Rb (10.11) 8 Bnr	several	14	GROPP	Rb (4.10) 8 Tu	Castle-	19	ADOLPH
Rb (4.12) 9 Bnr	Alpine		et al.	Rb (6.13) 9 Tu	town,		and
Rb (1.10) 10 Bnr	valleys,		1972	Rb (9.12) 10 Tu	Caithness		KLEIN
Rb (2.14) 11 Bnr	Bondo,			Rb (11.17)			1981;
Rb (7.8) 12 Bnr	Roveredo,			Rb (10.14)			BROOKER
Rb (13.16) 13 Bnr	Chiavenna			Rb (4.8)			1982
Rb (2.4) 67 Lub	Luino,	15	GROPP	Rb (1.11)			
Rb (3.8) 68 Lub	Northern,		et al.	Rb (8.17)			
Rb (6.7) 69 Lub	Italy		1982	Rb (8.14)			
Rb (5.13) 70 Lub				Rb (15.17)			
Rb (10.12) 71 Lub				Rb (3.8)			
Rb (9.14) 72 Lub				Rb (8.15)			
Rb (11.18) 73 Lub				Rb (3.16)			
Rb (16.17) 74 Lub				Rb (17.18)			
Rb (4.12) 1 Tu	several	16	ADOLPH	Rb (11.14)			
Rb (2.15) 2 Tu	places in		and	Rb (4.14) 11 Tu	places	20	ADOLPH
Rb (3.6) 3 Tu	Southern		KLEIN	Rb (5.15) 12 Tu	near		and
Rb (8.17) 4 Tu	Germany		1981; 1983	Rb (6.10) 13 Tu	Barcelona		KLEIN
Rb (10.14) 5 Tu				Rb (9.11) 14 Tu			1981
Rb (11.13) 6 Tu				Rb (12.13) 15 Tu			
Rb (5.15) 16 Tu							
Rb (13.14) 17 Tu				Rb (13.16) 1 Mpl	Ibiza	21	BRITTON-
Rb (5.14) 18 Tu							DAVIDIAN
Rb (1.5) 19 Tu							1983
Rb (3.8) 20 Tu							
Rb (6.10) 21 Tu				Rb (1.11) 2 Mpl	Monastir	22	SAID et al.
Rb (7.18) 22 Tu				Rb (2.16) 3 Mpl			1986
Rb (8.10) 23 Tu				Rb (3.12) 4 Mpl			
Rb (9.14) 24 Tu				Rb (4.6) 5 Mpl			
Rb (10.14) 25 Tu				Rb (5.14) 6 Mpl			
Rb (11.16) 26 Tu				Rb (7.18) 7 Mpl			
Rb (4.12) 1 Nam	Belgium	17	HÜBNER	Rb (8.9) 8 Mpl			
			1985	Rb (10.17) 9 Mpl			
Rb (3.14) 7 Tu	Orkney	18	ADOLPH	Rb (13.15) 10 Mpl			
Rb (4.10) 8 Tu	islands		and KLEIN				
Rb (9.12) 10 Tu			1981;				
Rb (6.14)			BROOKER				
			1982				

Some Rb chromosomes with similar arm composition as those observed in laboratory stocks were found in natural house mouse populations demonstrating that translocation events independently can occur involving the same chromosomes. Another point of interest is that some Rb's of laboratory mice have been found in strains already containing a metacentric derived from a feral mouse (GROPP and WINKING 1981). This leads to the conclusion that the introduction of preexisting Rb metacentric chromosomes into the laboratory genome is not essential for the occurrence of Robertsonian changes in laboratory strain. However, it may facilitate or enhance the generation of this type of chromosomal rearrangement.

Considerably higher numbers of Rb translocation chromosomes have been found in populations of wild living house mice. Together with the three Rb metacentrics from Dalmatia and Greece described in this report the total number of Rb chromosomes with

different arm composition amounts to 77. A list of update completeness recording all so far described Rb chromosomes using the current designation according to the arm composition and the nomenclature rules (see: GROPP and WINKING 1981) is shown in Table 5. 42 Rb metacentrics were observed in only one population or geographic site, whereas 35 Rb chromosomes were found at least twice and up to ten times with a mean occurrence of 2.1.

Table 5. Composition and frequency of Rb translocations in karyotypically distinct populations of feral mice. Rb translocations of laboratory origin are marked by an asterisk

Compo- sition	Frequency	Compo- sition	Frequency	Compo- sition	Frequency	Compo- sition	Frequency
1.2	2	3.10	1	6.10	2	10.11	2
1.2*	1	3.12	1	6.12	2	10.12	8
1.3	3	3.13	1	6.13	2	10.14	5
1.5	1	3.14	1	6.13*	1	10.14*	1
1.6	1	3.15*	1	6.14	1	10.15	1
1.7	1	3.16	1	6.15*	1	10.17	1
1.10	1	3.X*	1	6.16	2	11.13	7
1.11	3	4.6	4	6.19*	1	11.14	1
1.15*	1	4.8	1	7.8	2	11.14*	1
1.18	1	4.10	2	7.13*	1	11.15	1
2.3*	1	4.11	1	7.18	4	11.16	1
2.4	2	4.12	3	8.9	1	11.16	1
2.5	1	4.13	1	8.10	1	11.17	1
2.6*	1	4.14	1	8.12	2	11.18	1
2.8	4	4.15	1	8.14	3	12.13	1
2.14	1	4.15*	1	8.15	1	12.13*	1
2.15	1	4.17	1	8.17	4	12.14	1
2.16	1	4.18*	1	8.17*	1	13.14	1
2.17	1	5.12	1	8.19*	1	13.15	1
2.17*	1	5.13	3	9.11	1	13.16	2
2.18	1	5.14	3	9.12	2	15.17	2
3.4	3	5.15	10	9.13	1	16.17	7
3.5*	1	5.17	1	9.14	8	17.18	1
3.6	2	5.19*	1	9.16	3		
3.8	4	6.7	3	9.19*	1		
3.9	2						

The most frequent and widely distributed Rb chromosomes are 5.15, 10.12, 9.14, 11.13 and 16.17 which were observed in seven or more different karyotypes. Similarly composed metacentrics in karyotypically distinct populations pose the question of whether they are derived by spread from one source or from multiple independent mutational events. Yet, the answer must remain open as long as definitive markers along the Rb chromosomes or genetic tests for the precise ascertainment of identity or diversity are not available. However, from the geographical distribution patterns it can be inferred that spreading of Rb chromosomes is in majority, though not all cases, a likely explanation (GROPP et al. 1982). Even the presence of three similarly composed metacentrics in the populations near Zadar (Yugoslavia) and Palermo (Sicily) might be attributable to accidental introduction, e.g. by naval trade routes. It is possible that several new Rb chromosomes arose or accumulated independently after an initial spread of founder Rb metacentrics but a mutual spread between preexisting multimetacentric populations is similarly possible. In this respect and with regard to spread by sea traffic, it is interesting to note that the population with metacentric chromosomes near Zadar is limited to a coastal area surrounded by populations with only acrocentric chromosomes (DULIĆ et al. 1980). The origin of mouse populations with Rb metacentric chromosomes outside Italy can be suspected to have

occurred in coastal areas of Greece, Spain, Scotland and Tunisia suggesting accidental spread of Rb translocations into foreign populations via boat traffic. Interestingly Rb chromosomes are frequent in some parts of the British Isles (ADOLPH and KLEIN 1981), which, as proposed by DAVIS (1982), have been settled by continental mice via Vikings. It is likewise conceivable that the mutational events leading to the formation of banded chromosomes have taken place under the force of mixed genetic background of local and foreign genes. The finding of a "new" Rb chromosome in a Japanese population that showed signs of contamination with European house mice, is in favour of this hypothesis (MORIWAKI et al. 1984). Although Rb populations of the house mouse occur in many countries in Europe, the accumulation of Rb translocation chromosomes is most advanced in Italy. Altogether 11 populations with seven or more pairs of Rb chromosomes have been described. Similarly high numbers were only occasionally found outside Italy as in Tunisia. Under the viewpoint of time, the origin or introduction of Rb chromosomes in populations outside Italy is supposed to be more recent. This assumption is supported by the fact that the majority of populations with Rb translocations outside Italy, e.g. Greece, Spain, Southern Germany or Scotland is heterozygous or shows only lower numbers of Rb metacentrics. It has been claimed that Rb heterozygosity in natural populations plays an important role as a potent barrier and isolating mechanism between Rb and non Rb containing populations (WHITE 1978). This belief is based on the fact, that after introduction of ferally derived Rb chromosomes into a laboratory mouse genome heterozygous Rb carriers show an impaired fertility (TETTENBORN and GROPP 1970; CATTANACH and MOSELEY 1973; GROPP et al. 1974). This characteristic has been attributed to natural Rb-hybrids as well. The proof of unimpaired fertility of the natural hybrid of Zadar may indicate, that heterozygosity of at least some Rb chromosomes within their environmental genome does not have a negative effect upon fertility that is present after the introduction of the ferally derived Rb chromosome into a laboratory mouse genome (see Table 3). Since at the present time no real proof exists of a detrimental effect of Rb heterozygosity in natural hybrids, the role of chromosomes as an isolating mechanism and hence in the process of speciation has to be reconsidered.

The great number of variable composed Rb chromosomes in natural populations of the house mouse might lead to the assumption of a random involvement of all 19 acrocentric chromosomes of the mouse in the mutational process of Robertsonian centric translocations. Yet, an evaluation of frequency of involvement of each one of the acrocentric elements of the mouse karyotype in the 77 known Rb metacentrics shows (Fig. 3) that some are very frequently represented, as e.g. chromosome 10, 12 and 14, whereas others like no 7 and 18 participate only occasionally in the formation of Rb chromosomes, and chromosome 19 is, at least in feral house mice, never involved as it is with the sex chromosomes. It follows that certain chromosomes are more susceptible for the hypothetical mechanism which induces or facilitates the events of Rb translocations. If this assumption is correct, a sequential order of autosomes involved in Rb translocations has to be postulated. Although there is no definitive way to assess the subsequent changes in Rb accumulating natural populations, the comparison of Rb population with low and high numbers of translocated chromosomes can provide some hints for the elucidation of this problem. For example, Rb chromosomes with autosomes nos. 7 or 18 involved are found mostly in populations with high numbers (8 to 9 pairs) of Rb chromosomes, whereas autosomes 12 and 10 as one arm of a Rb chromosome are represented almost in all Rb-populations, even in populations with low numbers of mutated chromosomes (1 to 3 pairs). Although the numbers of metacentric chromosomes of laboratory mouse strains are low, a similar nonrandom involvement of autosomes does not seem to exist.

What may be the reason for the differential proneness of individual chromosomes of the wild mouse genome to be involved in centric translocations? MILLER et al. (1978) have pointed out that nucleolus organizer regions (NORs) do have some influence upon the



Fig. 3. Percentage of each chromosome of the standard karyotype as one part of individual Rb translocations in different populations of feral mice from Europe and Northern Africa. The calculation is based on data of 22 mouse populations (see Tab. 4 and Fig. 2). Values above 100 % result from multiple involvement of certain autosomes in Rb heterogeneous populations (see Tab. 4, populations 15, 16 and 19). NOR bearing chromosomes are marked with an arrow

frequency of Rb translocations, since in mouse cell lines chromosomes with active NORs are significantly overrepresented in Rb chromosomes. From laboratory mice it is known that chromosomes 12, 15, 16, 18 and 19 may bear NORs proximal to the centromeric heterochromatin. In metaphases of European wild mice silver NORs appear at the same chromosomes and locations, although the presence of silver NORs is variable between feral mouse populations (WINKING et al. 1980). The high frequency of chromosomes 12 and 15 in Rb translocations of wild mice supports the data of MILLER et al. (1978). However, autosomes 18 and 19 carry silver NORs as well, but are by far the least represented partners in Rb translocations. This may indicate that other factors than NORs play the major role in the production of Rb translocations in feral mouse populations. Additional support of this view comes from the fact that Rb chromosomes with rRNA gene clusters on both sites of the centromere are lacking among the collection of Rb translocations in feral mice. Theoretically the only candidates could have been the combinations 15.17 and 16.17 of European wild mice, but the presence of NORs on chromosome 17 has only been documented in the Asian subspecies *M. m. molossinus* (DEV et al. 1977). A further point, which might be of importance for the generation of Rb chromosomes, is the organization of the region intimately connected with the process of Rb rearrangement. From cytological observations it becomes clear that the breakpoints prior to translocation are located within the paracentromeric heterochromatin or C-band positive material (GROPP and WINKING 1981). Heterogeneity of this region in respect of

base pair composition has been ascertained between individual chromosomes of laboratory mice (THUST and RONNE 1980) and chromosomes of mouse cell lines (MARCUS et al. 1980) as well as between species of the genus *Mus* (SEN and SHARMA 1980; BROWN and DOVER 1980). Whether these differences are causally related to the different proneness of chromosomes within the species *Mus* and between species of the genus *Mus* to undergo the process of Rb rearrangement is not yet clear and should be elucidated in further experiments.

Acknowledgement

In memoriam of Prof. Dr. ALFRED GROPP, who discovered the Robertsonian polymorphism of feral mice and made possible these findings.

Zusammenfassung

Karyotypvariation durch Robertsonsche Translokationschromosomen bei der europäischen Hausmaus, Mus musculus. Eine Übersicht über den derzeitigen Wissensstand und neue Informationen

Untersucht wurde der Karyotyp der langschwänzigen Hausmaus, *Mus musculus*, aus Zadar (Jugoslawien) und Ammoudia (Griechenland). In Zadar konnten sechs und in Ammoudia drei Robertsonsche (Rb) Chromosomen nachgewiesen und mit Hilfe der G-Banden identifiziert werden. Die Komposition der Markerchromosomen war teils neu, teils in anderen, geographisch getrennten Populationen schon gefunden worden. Die karyologischen Befunde dieser beiden Populationen aus dem osteuropäischen Verbreitungsgebiet werden gemeinsam mit Beobachtungen zum Karyotyp mittel- und westeuropäischer sowie nordafrikanischer Hausmauspopulationen diskutiert.

Die Fertilitätsdaten eines männlichen Wildfanges mit einer Rb-Heterozygotie lassen den Schluß zu, daß dieser Genotyp in Wildmäusen nicht mit einer Fertilitätseinbuße gekoppelt sein muß, wie sie in Wildmaus/Labormaus-Hybriden infolge von Meiosestörungen mit anschließender Bildung befruchtungsfähiger, aber aneuploider Gameten hinreichend dokumentiert ist.

References

- ADOLPH, S.; KLEIN, J. (1981): Robertsonian variation in *Mus musculus* from Central Europe, Spain, and Scotland. *J. Hered.* **72**, 219–221.
- ADOLPH, S.; KLEIN, J. (1983): Genetic variation of wild mouse populations in Southern Germany. *Genet. Res.* **41**, 117–134.
- ARROYO NOMBELA, J. J.; RODRIGUEZ MURCIA, C. (1977): Spontaneous double Robertsonian translocation (Rb2.3) and Rb(X.3) in the mouse. *Cytogenet. Cell Genet.* **19**, 227–230.
- BARANOV, V. S.; DYBAN, A. P. (1971): Embryogenesis and peculiarities of karyotype in mouse embryos with centric fusion of chromosomes (Robertsonian translocation). *Ontogenez.* **2**, 164–176.
- BRITTON-DAVIDIAN, J. (1983): Private communication. *Mouse News Letter* **69**, 35.
- BROOKER, P. C. (1982): Robertsonian translocations in *Mus musculus* from N.E. Scotland and Orkney. *Heredity* **48**, 305–309.
- BROWN, S. D. M.; DOVER, G. (1980): Conservation of segmental variants of satellite DNA of *Mus musculus* in a related species: *Mus spretus*. *Nature* **258**, 47–49.
- CAPANNA, E.; GROPP, A.; WINKING, H.; NOACK, G.; CIVITELLI, M.-V. (1976): Robertsonian metacentrics in the mouse. *Chromosoma* **58**, 341–353.
- CATTANACH, B. M.; MOSELEY, M. (1973): Nondisjunction and reduced fertility caused by the tobacco mouse metacentric chromosomes. *Cytogenetics* **12**, 264–287.
- CHAKRABARTI, S.; CHAKRABARTI, A. (1977): Spontaneous Robertsonian fusion leading to karyotype variation in the mouse. – First report from Asia. *Experientia* **33**, 175.
- COMMITTEE ON STANDARDIZED GENETIC NOMENCLATURE FOR MICE (1979): New rules for nomenclature of genes, chromosome anomalies and inbred strains. *Mouse News Letter* **61**, 4–16.
- DAVIS, S. J. M. (1982): Wild mouse morphometrics. Private communication. *Mouse News Letter* **66**, 79–80.
- DEV, V. G.; TANTRAVAH, R.; MILLER, D. A.; MILLER, O. J. (1977): Nucleolus organizers in *Mus musculus* subspecies and in the RAG mouse cell line. *Genetics* **86**, 389–398.
- DULIĆ, B.; SOLDATOVIC, B.; DUNDERSKI, Z. (1980): Distribution of karyotypes in *Mus musculus* Linnaeus, 1758 (Rodentia, Muridae) in some regions of Yugoslavia. *Biosistematika* **6**, 203–210.
- EVANS, E. P.; LYON, M. F.; DAGLISH, M. (1967): A mouse translocation giving a metacentric marker chromosome. *Cytogenetics* **6**, 105–119.

- EVANS, E. P. (1976): Male sterility and double heterozygosity for Robertsonian translocations in the mouse. In: *Chromosomes Today*. Ed. by P. L. PEARSON and K. R. LEWIS. New York: Wiley and Sons. Vol. 5, 75–81.
- FERRIS, S. D.; SAGE, R. D.; WILSON, A. C. (1982): Evidence from mtDNA sequences that common laboratory strains of inbred mice are descended from a single female. *Nature* **295**, 163–165.
- GROPP, A.; TETTENBORN, U.; v. LEHMANN, E. (1970): Chromosomenvariation vom Robertsonschen Typus bei der Tabakmaus, *M. poschiavinus* und ihren Hybriden mit der Laboratoriumsmaus. *Cytogenetics* **9**, 9–23.
- GROPP, A.; WINKING, H.; ZECH, L.; MÜLLER, H. J. (1972): Robertsonian chromosomal variation and identification of metacentric chromosomes in feral mice. *Chromosoma* **30**, 265–288.
- GROPP, A.; GIER, D.; KOLBUS, U. (1974): Trisomy in the fetal backcross progeny of male and female metacentric heterozygotes of the mouse. *Cytogenet. Cell Genet.* **13**, 511–535.
- GROPP, A.; WINKING, H. (1981): Robertsonian translocations: Cytology, meiosis, segregation patterns and biological consequences of heterozygosity. *Symp. Zool. Soc. Lond.* **47**, 141–181. In: *Biology of the House Mouse*. Ed. by R. J. BERRY. London, New York: Academic Press.
- GROPP, A.; WINKING, H.; RED, C.; CAPANNA, E.; BRITTON-DAVIDIAN, J.; NOACK, G. (1982): Robertsonian karyotype variation in wild house mice from Rhaeto – Lombardia. *Cytogenet. Cell Genet.* **34**, 67–77.
- HÜBNER, R. (1985): A Robertsonian translocation in wild house mice from Belgium. *Mouse News Letter* **72**, 116–117.
- LEHMANN, E. v.; RADBRUCH, A. (1977): Robertsonian translocations in *Mus musculus* from Sicily. *Experientia* **33**, 1025–1026.
- LEONARD, A.; DEKNUDT, G. H. (1967): A new marker for chromosome studies in the mouse. *Nature, Lond.* **214**, 504–505.
- MARCUS, M.; NIELSEN, K.; GOITEIN, R.; GROPP, A. (1979): Pattern of condensation of mouse and chinese hamster chromosomes in G2 and mitosis of 33258-Hoechst treated cells. *Exp. Cell Res.* **122**, 191–201.
- MATTHEY, R. (1966): Le polymorphisme chromosomique des *Mus* africains du sous-genre *Leggada*. Revision generale portant sur l'analyse de 213 individus. *Revue suisse Zool.* **73**, 585–607.
- MILLER, O. J.; MILLER, D. A.; TANTRAHAHI, R.; DEV, V. G. (1978): Nucleolus organizer activity and the origin of Robertsonian translocations. *Cytogenet. Cell Genet.* **20**, 40–50.
- MORIWAKI, K.; YONEKAWA, H.; GOTOH, O.; MINEZAWA, M.; WINKING, H.; GROPP, A. (1984): Implications of the genetic divergence between European wild mice with Robertsonian translocations from the viewpoint of mitochondrial DNA. *Genet. Res., Camb.* **43**, 277–287.
- NESBITT, M. N.; FRANKE, U. (1973): A system of nomenclature for band patterns of mouse chromosomes. *Chromosoma* **41**, 145–158.
- ORSINI, P. PH.; BONHOMME, F.; BRITTON-DAVIDIAN, J.; CROSET, H.; GERASIMOV, S.; THALER, L. (1983): The complex of species of genus *Mus* in Central and Oriental Europe. II. Criteria for identification, distribution and ecological characteristics. *Z. Säugetierkunde* **48**, 86–95.
- ROBINSON, T. J. (1978): Preliminary report of a Robertsonian translocation in an isolated feral *Mus musculus* population. *Mamm. Chrom. Newsl.* **19**, 84–85.
- SAID, K.; JACQUART, T.; MONTGELARD, C.; SONJAYA, H.; HELAL, A. N.; BRITTON-DAVIDIAN, J. (1986): Robertsonian house mouse populations in Tunisia: A karyological and biochemical study. *Genetica* **68**, 151–156.
- SEABRIGHT, M. (1971): A rapid banding technique for human chromosomes. *Lancet* **II**, 971–972.
- SEARLE, A. G.; BEECHY, C. V.; EVANS, E. P. (1978): Meiotic effects in chromosomally derived male sterility of mice. *Ann. Biol. Anim. Biochem. Biophys.* **18**, 391–398.
- SEARLE, A. G.; BEECHY, C. V. (1986): Map of structural changes. *Mouse News Letter* **75**, 17.
- SEN, S.; SHARMA, T. (1980): Quantitative variation of “*Mus musculus*-like” constitutive heterochromatin and satellite DNA-sequences in the genus *Mus*. *Chromosoma* **81**, 393–402.
- TETTENBORN, U.; GROPP, A. (1970): Meiotic non-disjunction in mice and mouse hybrids. *Cytogenetics* **9**, 272–283.
- THALER, L.; BONHOMME, F.; BRITTON-DAVIDIAN, J. (1981): Process of speciation and semi-speciation in the house mouse. *Symp. Zool. Soc. Lond.* **47**, 27–41. In: *Biology of the House Mouse*. Ed. by R. J. BERRY. London, New York: Academic Press.
- THUST, R.; RONNE, M. (1980): Localization of AT-clusters in normal mouse chromosomes by netropsin prefixation treatment in vitro. *Hereditas* **93**, 321–326.
- TRIMAN, K. L.; DAVISSON, M. T.; RODERICK, T. H. (1975): A method for preparing chromosomes from peripheral blood in the mouse. *Cytogenet. Cell Genet.* **15**, 166–176.
- WHITE, M. J. D. (1978): Chain processes in chromosomal speciation. *Syst. Zool.* **27**, 285–298.
- WINKING, H.; NIELSEN, K.; GROPP, A. (1980): Variable positions of NORs in *Mus musculus*. *Cytogenet. Cell Genet.* **26**, 158–164.
- WINKING, H.; GROPP, A. (1983): Multimetacentric wild mouse (*M. musculus domesticus*) populations. *Mouse News Letter* **68**, 75.
- YONEKAWA, H.; MORIWAKI, K.; GOTOH, O.; WATANABE, J.; HAYASHI, J.-I.; MIYASHITA, N.; PETRAS,

- M. L.; TAGASHIRA, Y. (1980): Relationship between laboratory mice and the subspecies *Mus musculus domesticus* based on restriction endonuclease. *Jap. J. Genet.* 55, 289–296.
- ZIMMERMANN, K. (1949): Zur Kenntnis der mitteleuropäischen Hausmäuse. *Zool. Jb. (Syst.)* 78, 301–322.

Authors' addresses: Dr. HEINZ WINKING, Institut für Biologie der Medizinischen Universität zu Lübeck, Ratzeburger Allee 160, D-2400 Lübeck, FRG; Dr. BEATRICA DULIĆ, Institute of Biology, University of Zagreb, Rooseveltov Trg 6, YU-41000 Zagreb, Yugoslavia; Dr. GRAHAM BULFIELD, Institute of Animal Physiology and Genetics Research, Edinburgh Research Station, Roslin, Midlothian, EH25 9PS, Scotland

ZOBODAT - www.zobodat.at

Zoologisch-Botanische Datenbank/Zoological-Botanical Database

Digitale Literatur/Digital Literature

Zeitschrift/Journal: [Mammalian Biology \(früher Zeitschrift für Säugetierkunde\)](#)

Jahr/Year: 1988

Band/Volume: [53](#)

Autor(en)/Author(s): Winking Heinz, Dulic Beatrica, Bulfield Graham

Artikel/Article: [Robertsonian karyotype variation in the European house mouse, *Mus musculus* Survey of present knowledge and new observations 148-161](#)